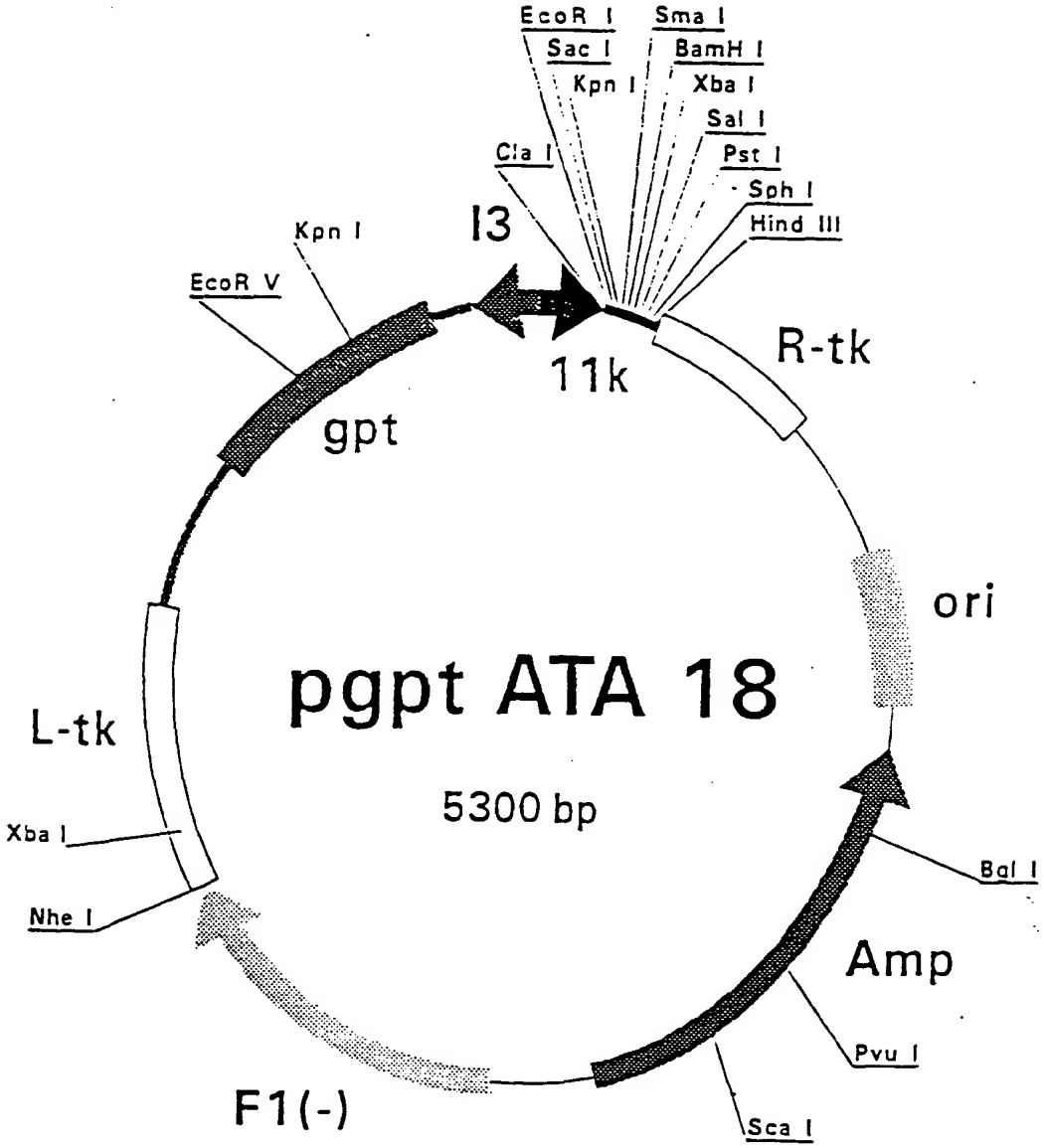

EcoR I
Sma I
Sac I
BamH I
Kpn I
Xba I
Sal I
Cla I
Pst I
Sph I
Hind III
I3
Kpn I
EcoR V
11k
R-tk
gpt
ori
pgpt ATA 18
5300 bp
L-tk
Xba I
Bgl I
Nhe I
Amp
Pvu I
F1(-)
Sca I

FIGURE 1

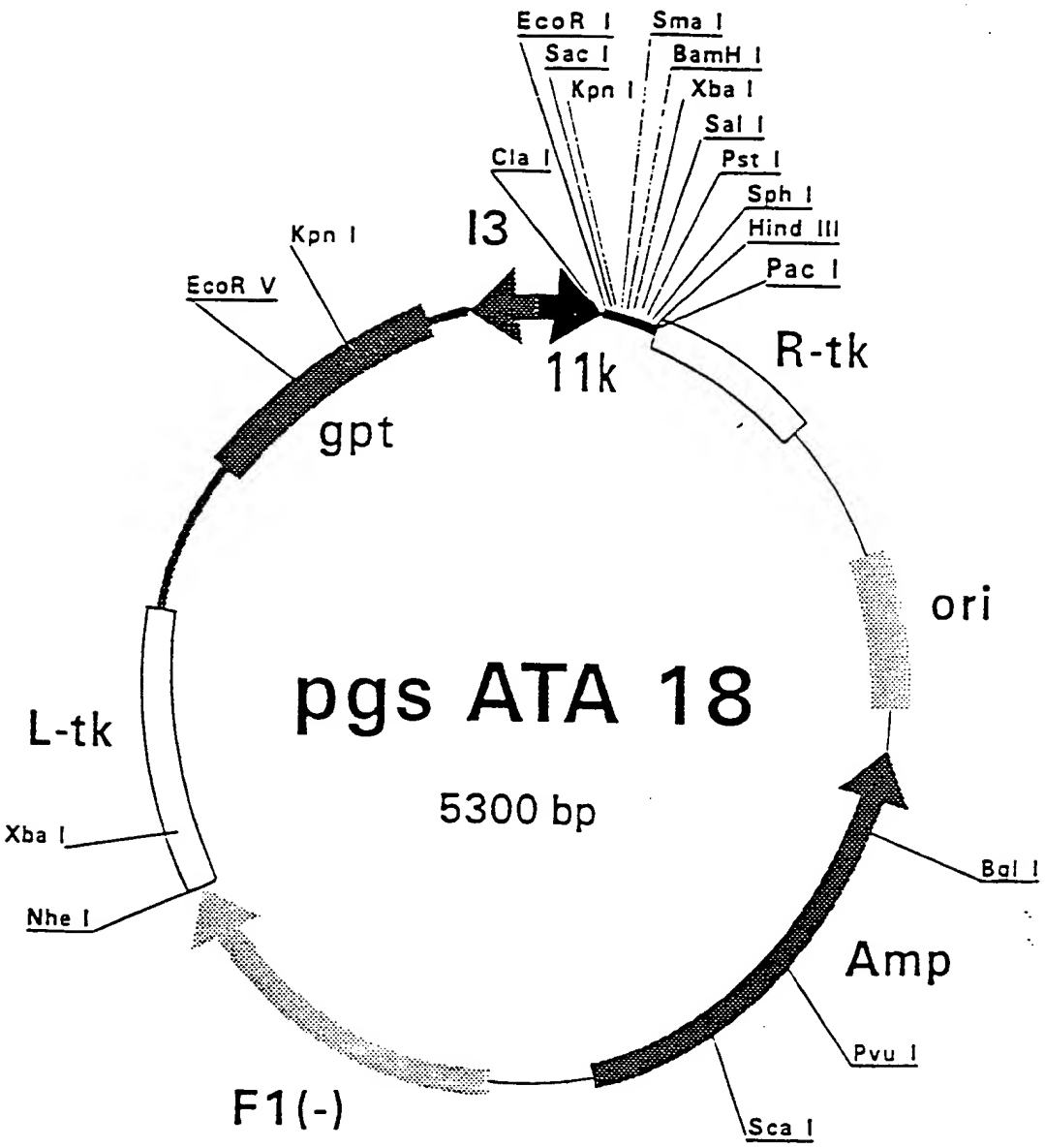

EcoR I
Sma I
Sac I
BamH I
Kpn I
Xba I
Sal I
Cla I
Pst I
Sph I
Hind III
Pac I
I3
Kpn I
EcoR V
11k
R-tk
gpt
ori
pgs ATA 18
5300 bp
L-tk
Xba I
Bgl I
Nhe I
Amp
Pvu I
F1(-)
Sca I

FIGURE 2

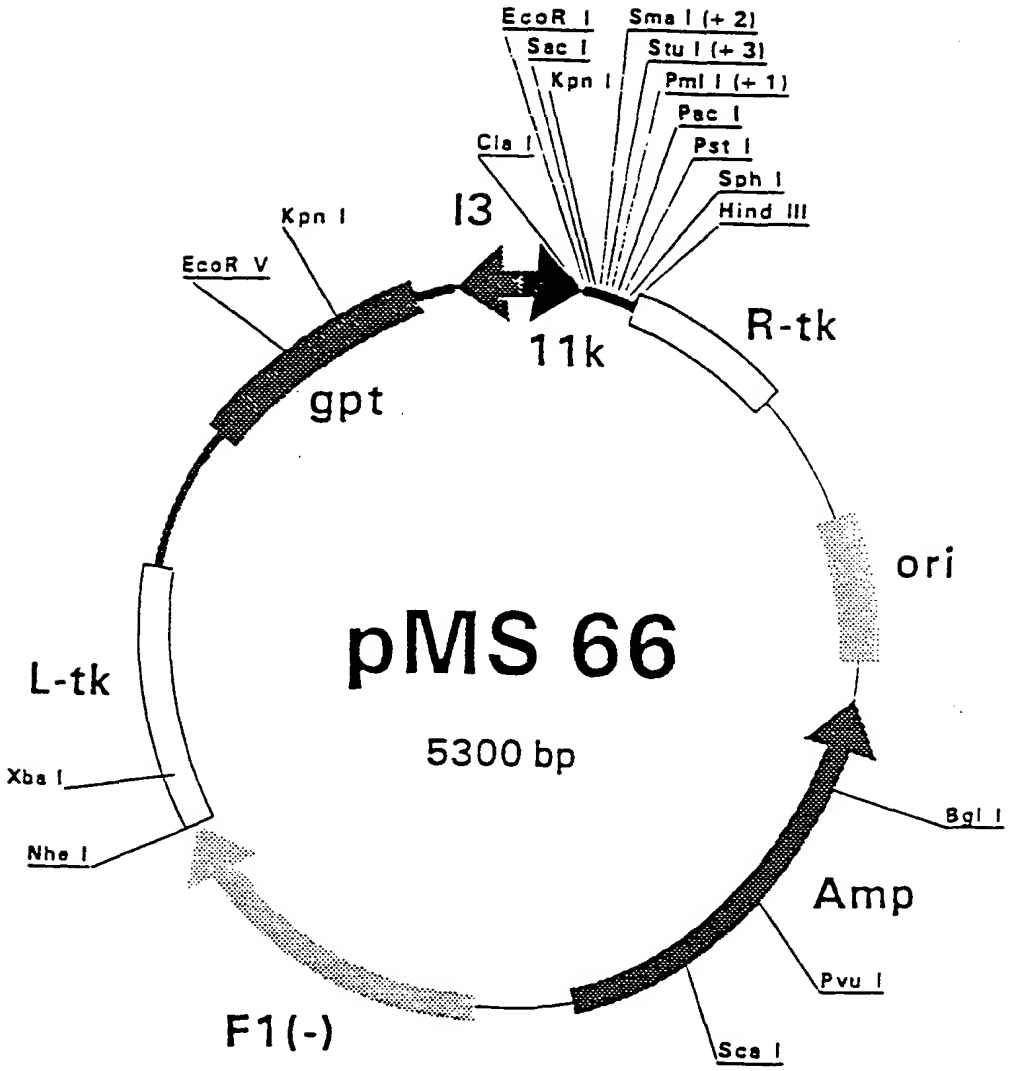

EcoR I
Sma I (+ 2)
Sac I
Stu I (+ 3)
Kpn I
Pml I (+ 1)
Pac I
Cla I
Pst I
Sph I
Hind III
I3
Kpn I
EcoR V
11k
R-tk
gpt
ori
pMS 66
5300 bp
L-tk
Xba I
Bgl I
Nhe I
Amp
Pvu I
F1(-)
Sca I

FIGURE 3

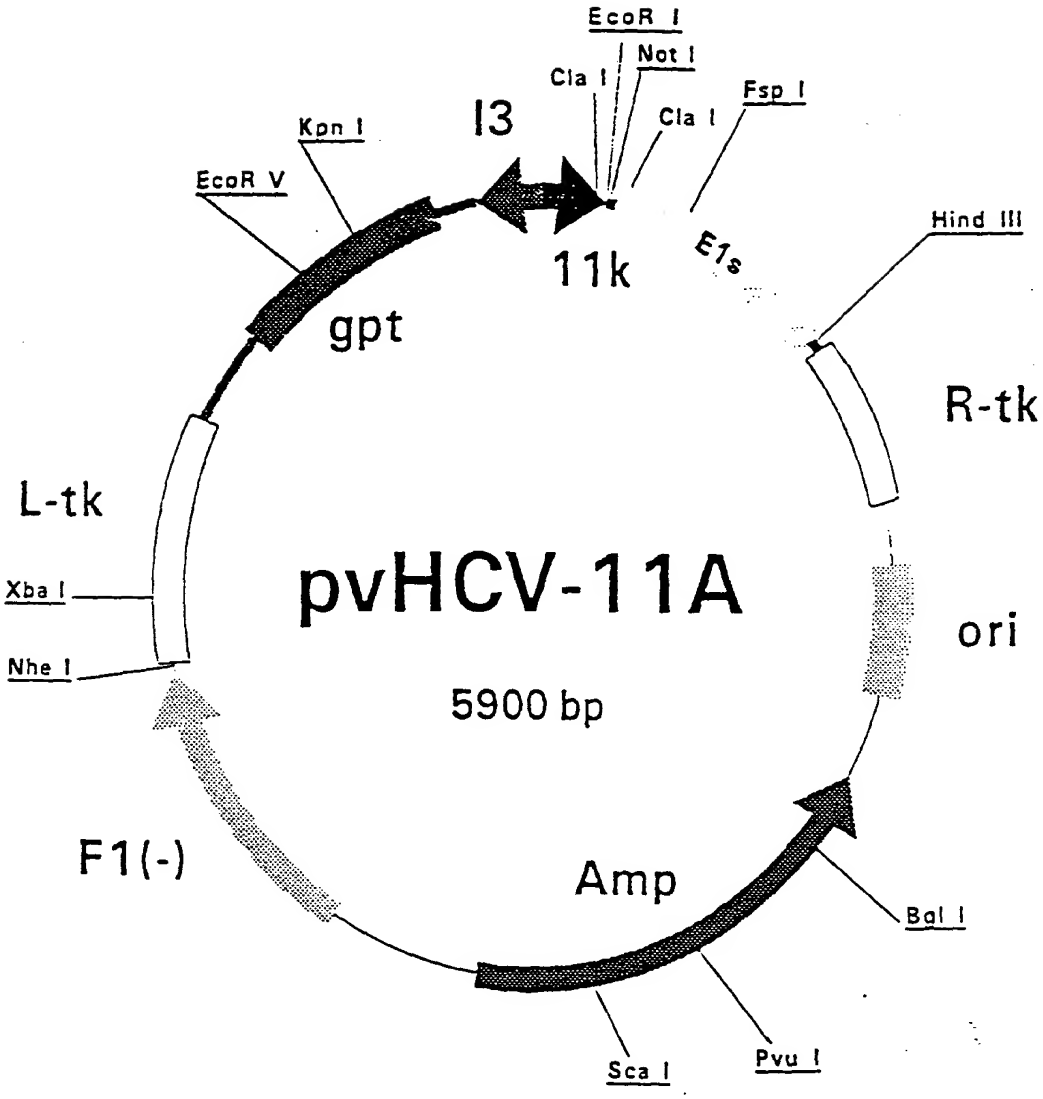

EcoR I
Not I
Cla I
Cla I
Fsp I
I3
Kpn I
EcoR V
11k
E1s
Hind III
gpt
R-tk
L-tk
pvHCV-11A
Xba I
ori
Nhe I
5900 bp
F1(-)
Amp
Bal I
Sca I
Pvu I

FIGURE 4

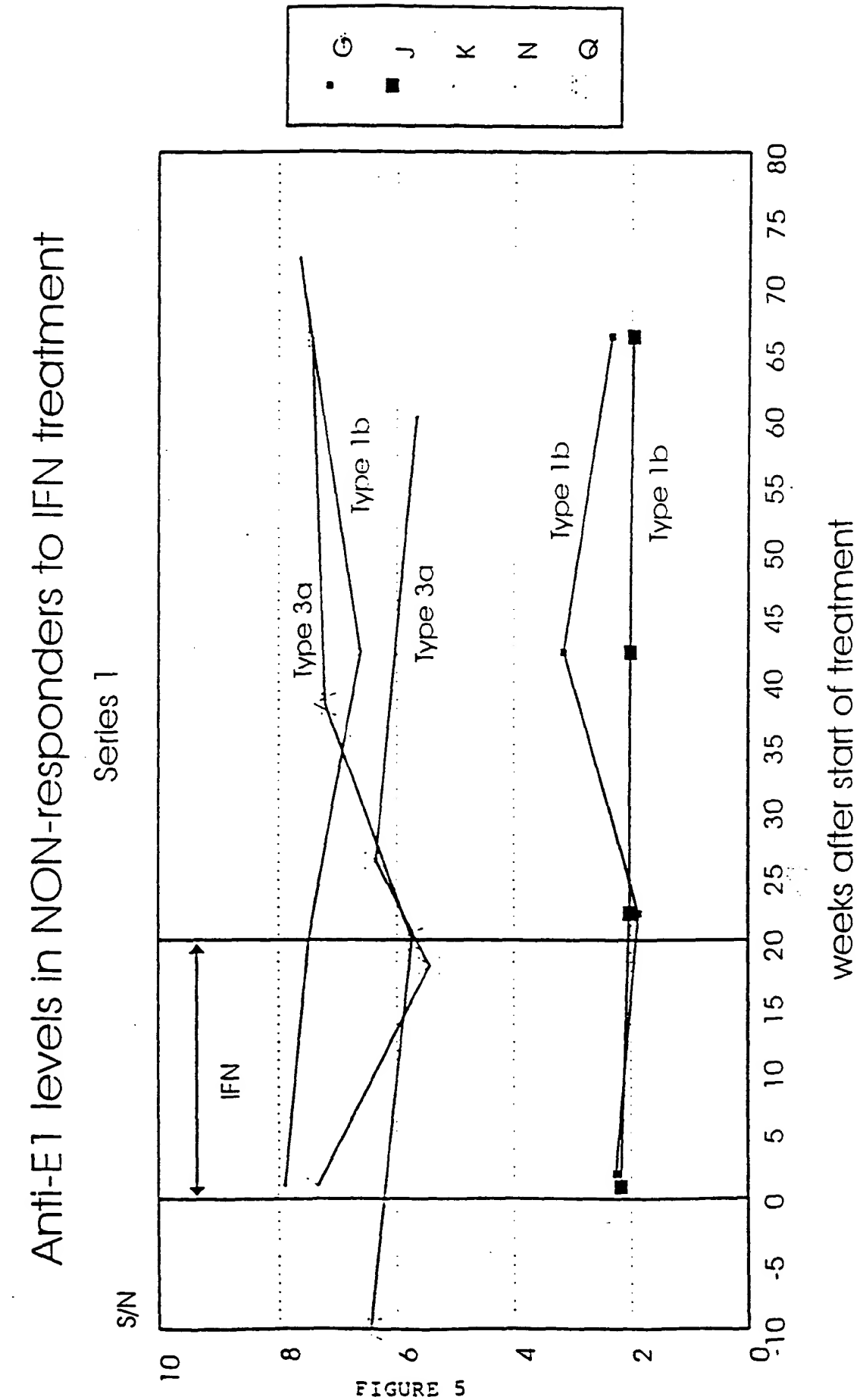
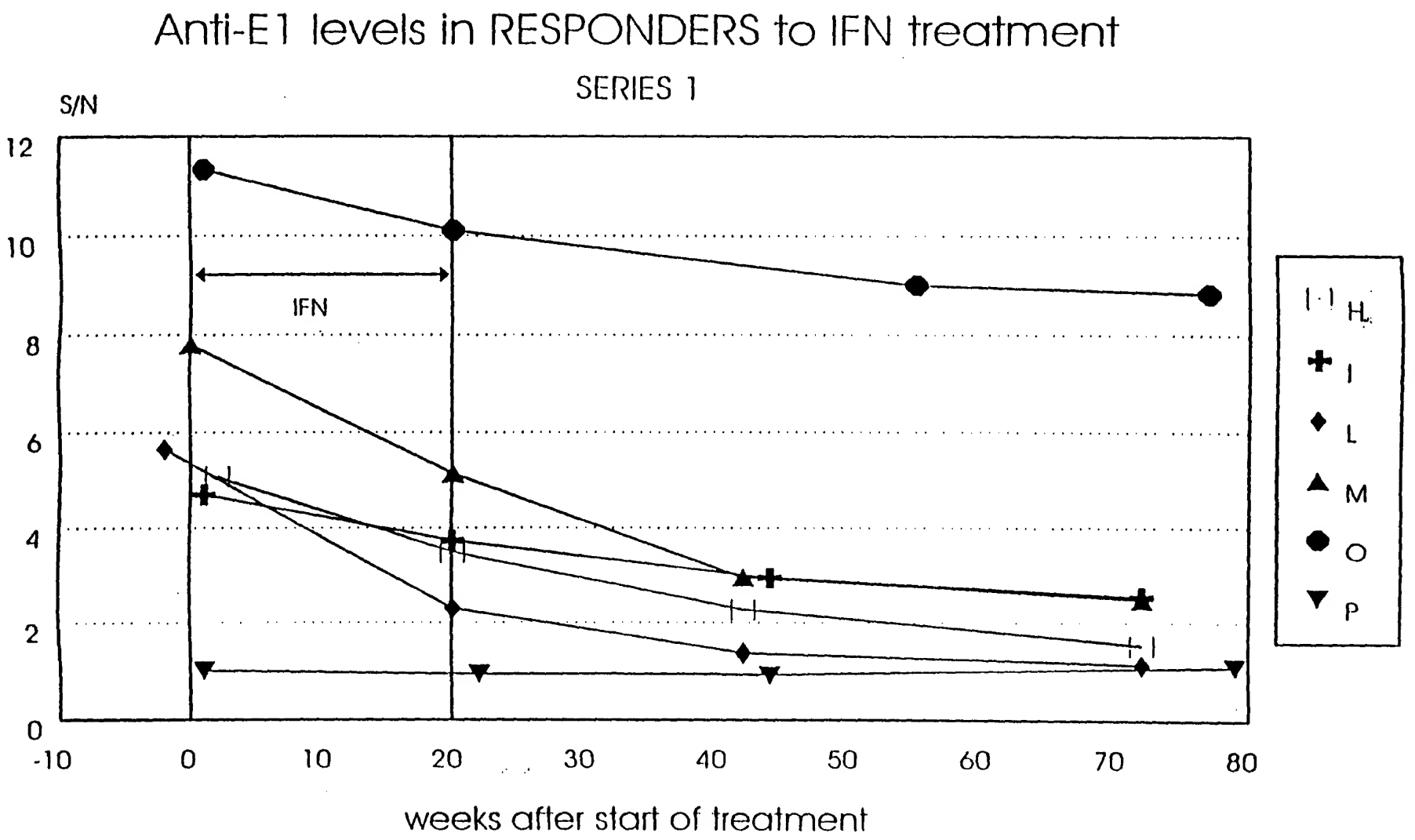

Anti-E1 levels in NON-responders to IFN treatment
Series 1
G
J
K
N
Q
S/N
10
8
6
4
2
0
-10
-5
0
5
10
15
20
25
30
35
40
45
50
55
60
65
70
75
80
IFN
Type 3a
Type 1b
Type 3a
Type 1b
Type 1b
weeks after start of treatment

FIGURE 5


Anti-E1 levels in RESPONDERS to IFN treatment
SERIES 1
S/N
12
10
8
6
4
2
0
-10
0
10
20
30
40
50
60
70
80
IFN
weeks after start of treatment
H
I
L
M
O
P

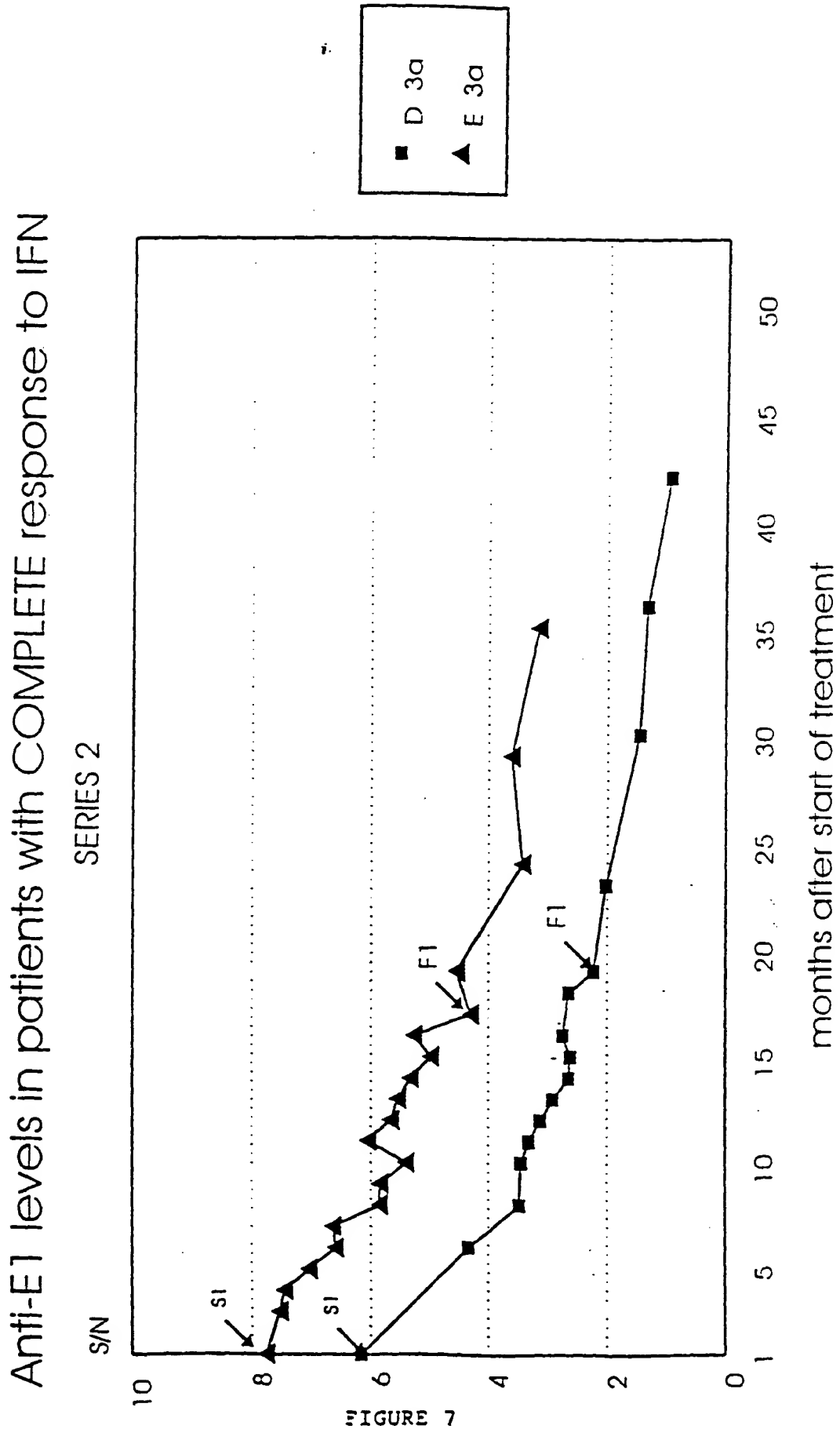
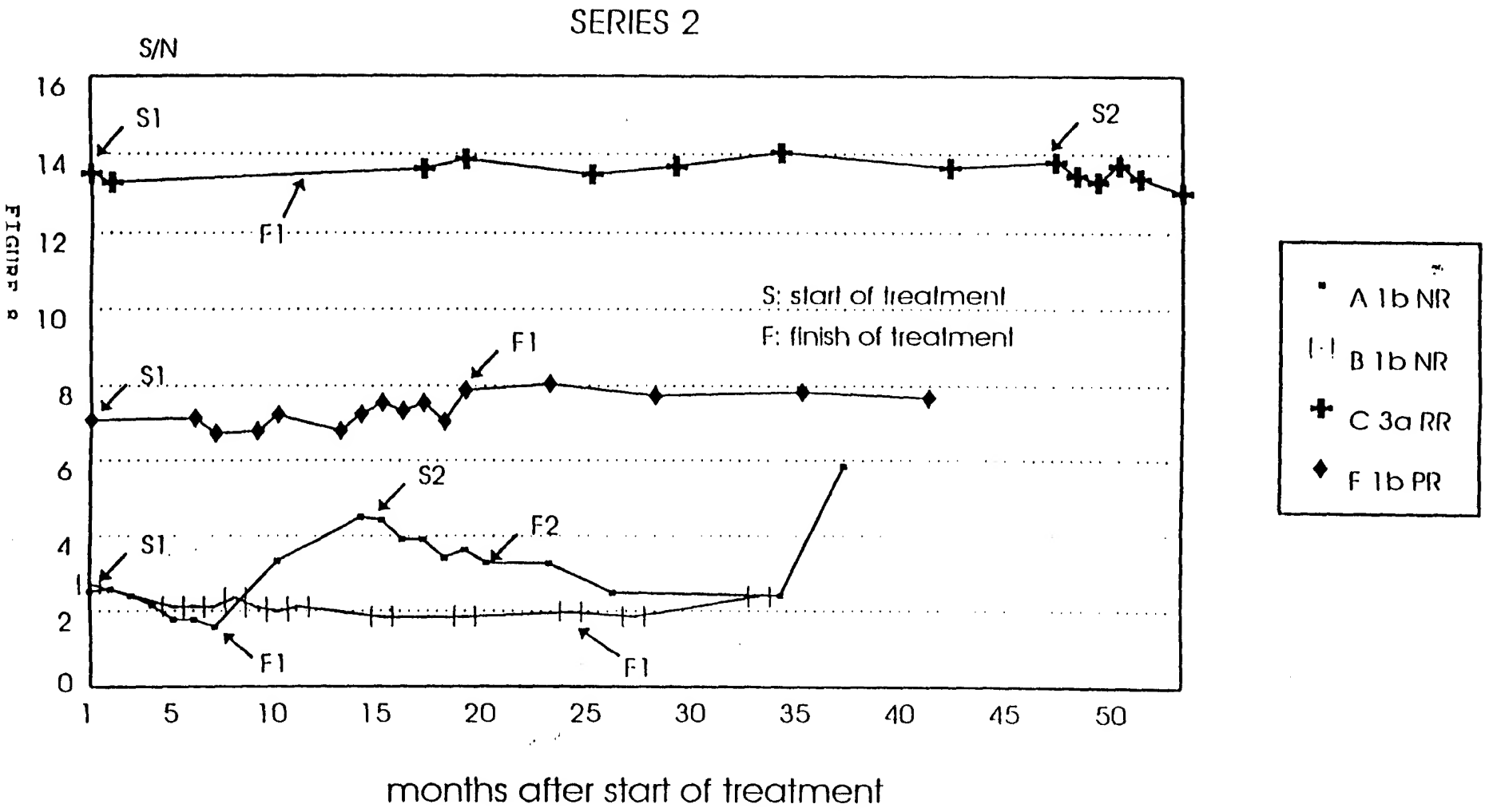

Anti-E1 levels in patients with COMPLETE response to IFN
SERIES 2
S/N
D 3a
E 3a
S1
S1
F1
F1
10
8
6
4
2
0
1
5
10
15
20
25
30
35
40
45
50
months after start of treatment

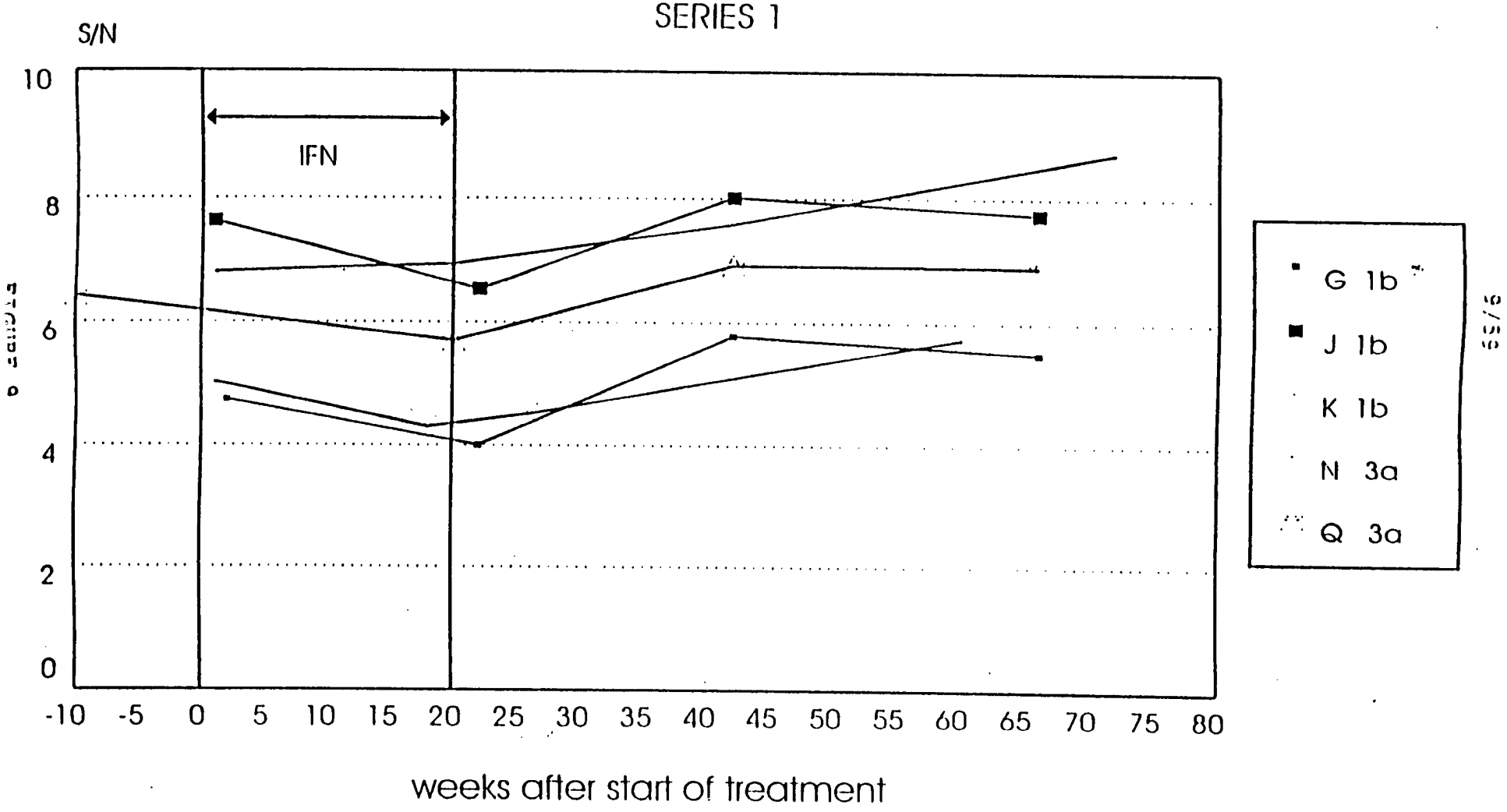
FIGURE 7

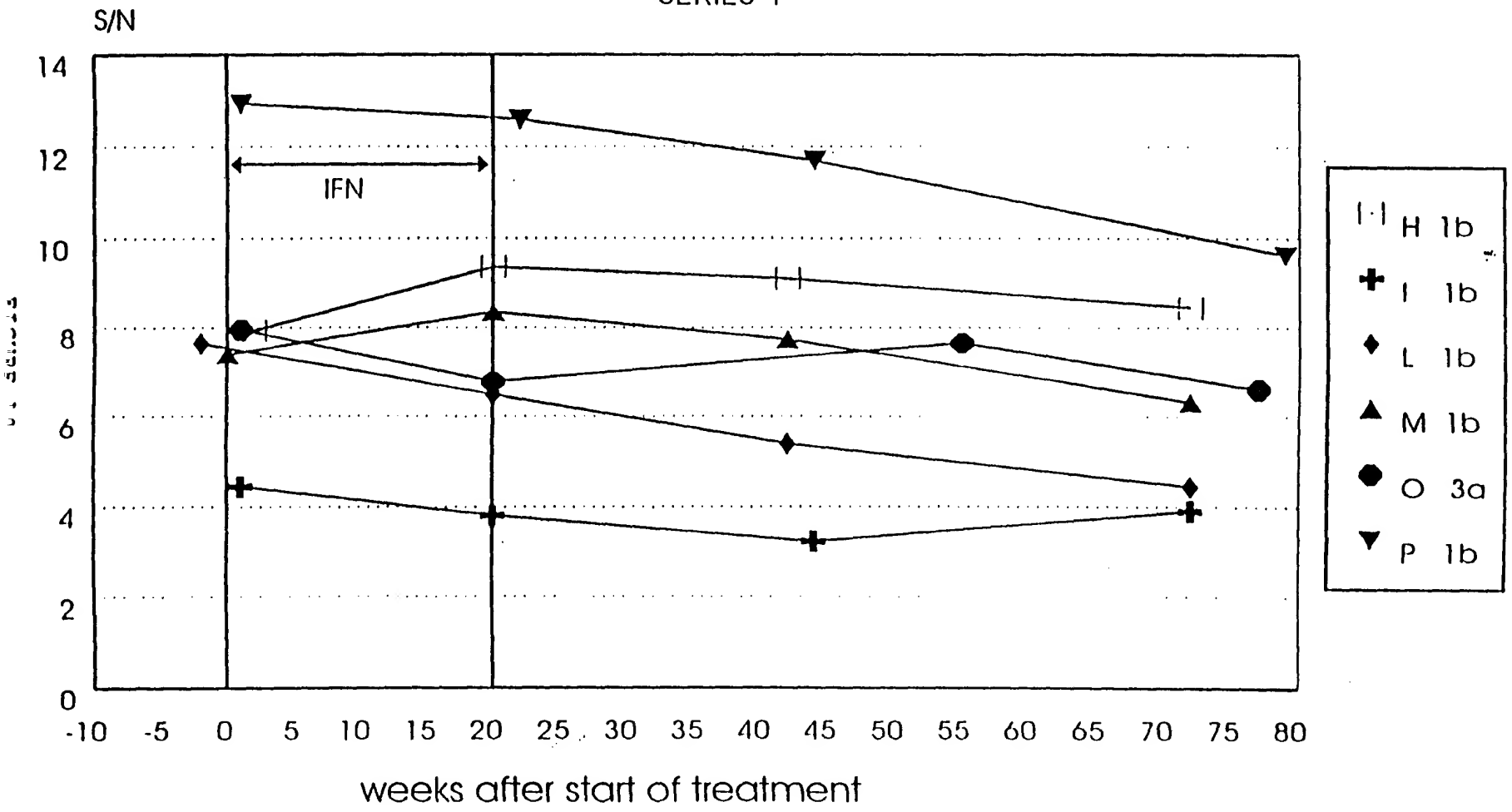
FIGURE 8

Anti-E1 levels in INCOMPLETE responders to IFN treatment



Anti-E2 levels in NON-RESPONDERS to IFN treatment




Anti-E2 levels in RESPONDERS to IFN treatment
SERIES 1
S/N
14
12
10
8
6
4
2
0
IFN
-10 -5 0 5 10 15 20 25 30 35 40 45 50 55 60 65 70 75 80
weeks after start of treatment
H 1b
I 1b
L 1b
M 1b
O 3a
P 1b

Anti-E2 levels in INCOMPLETE responders to IFN treatment

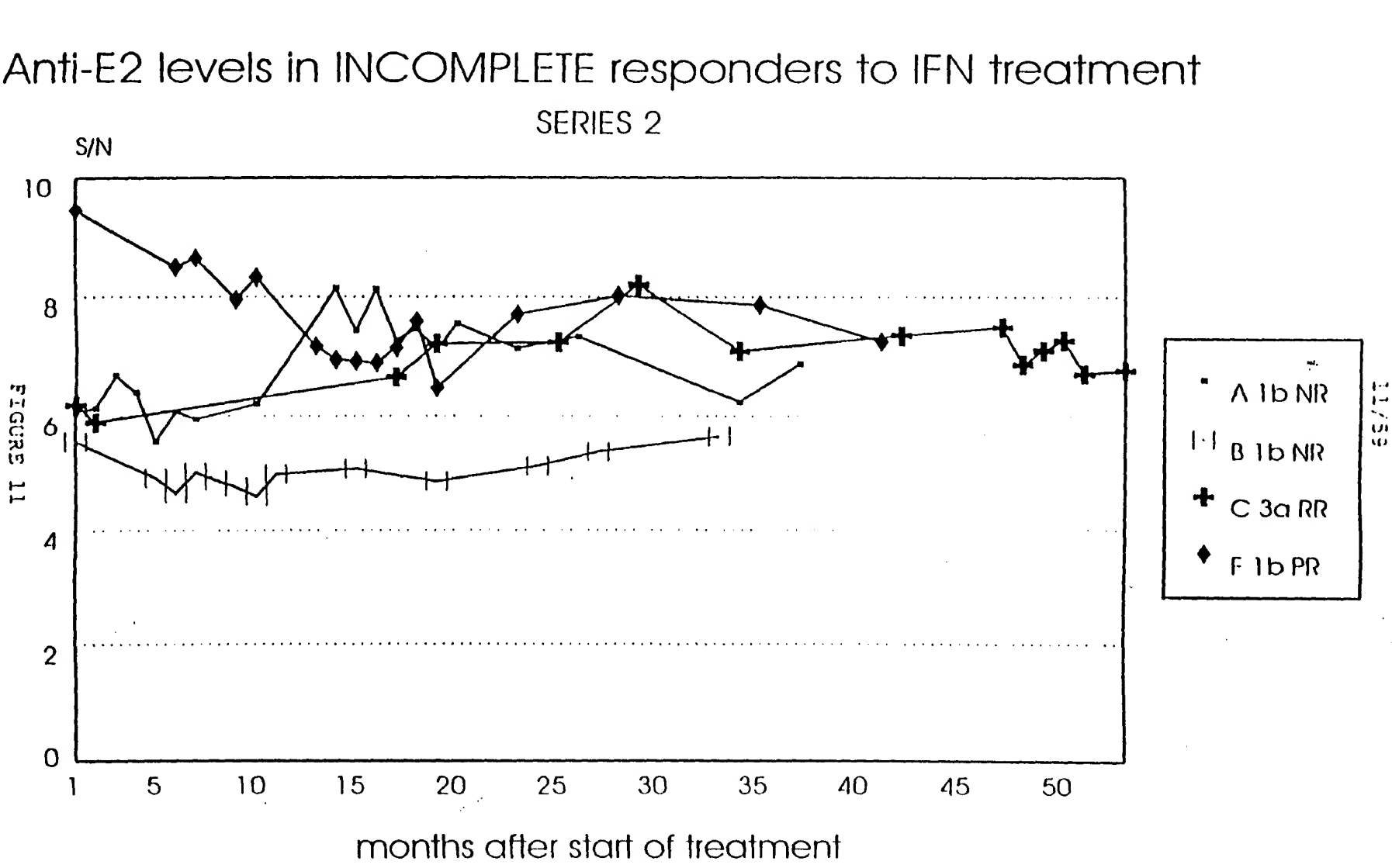


FIGURE 11/33

Anti-E2 levels in COMPLETE responders to IFN treatment

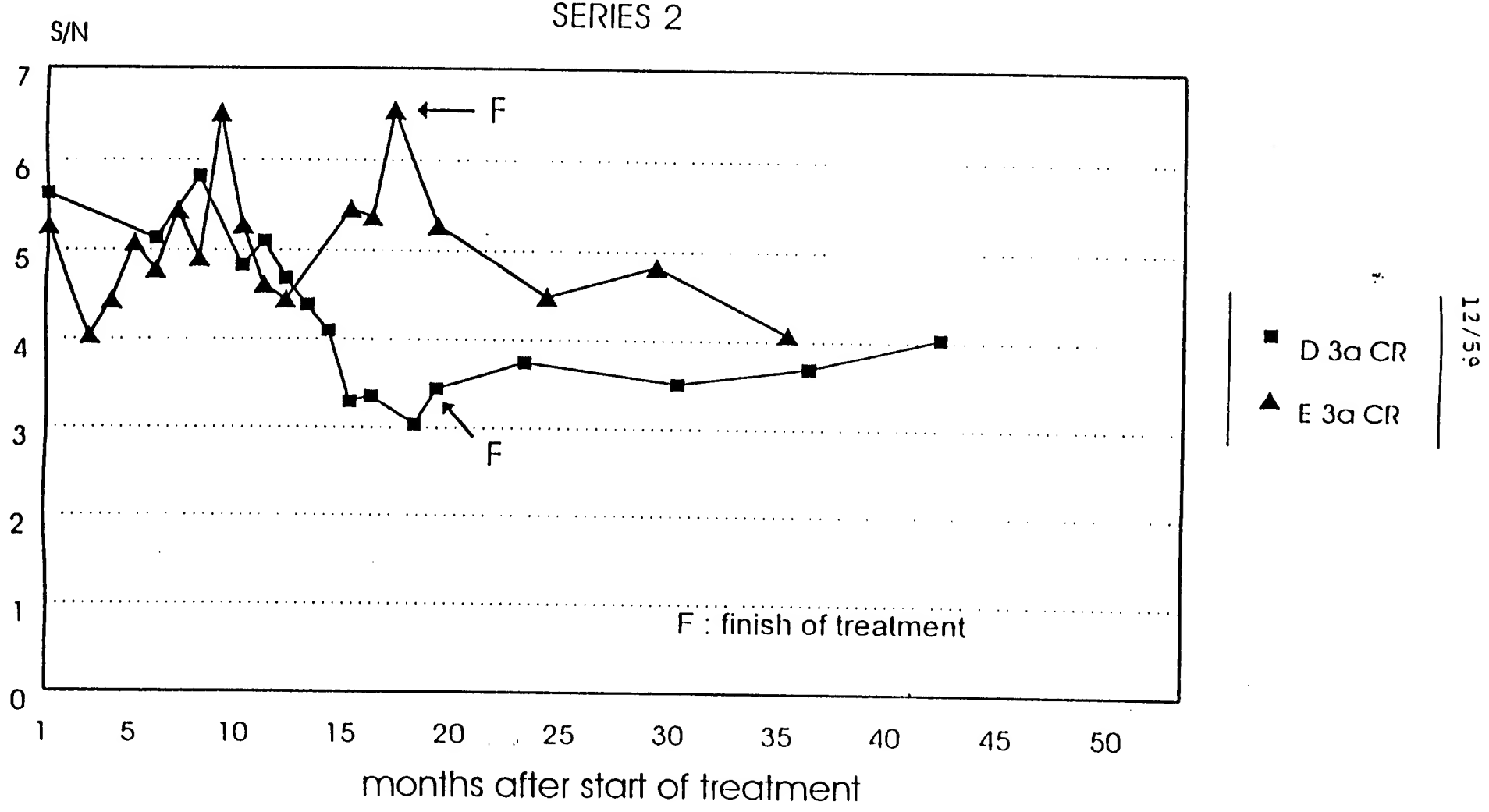


FIGURE 12

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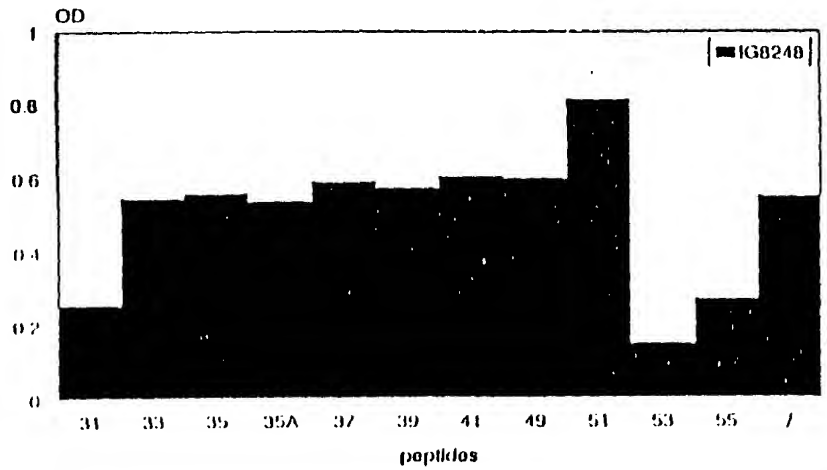
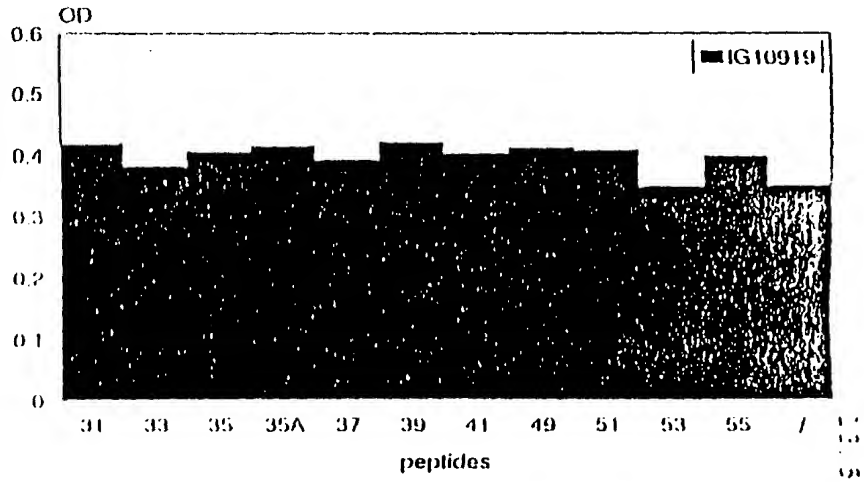
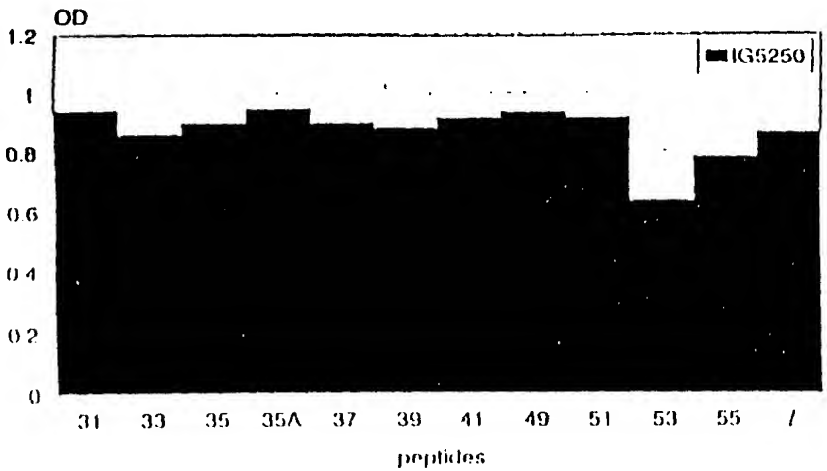
FIGURE 13

Human anti-E1 reactivity competed with peptides







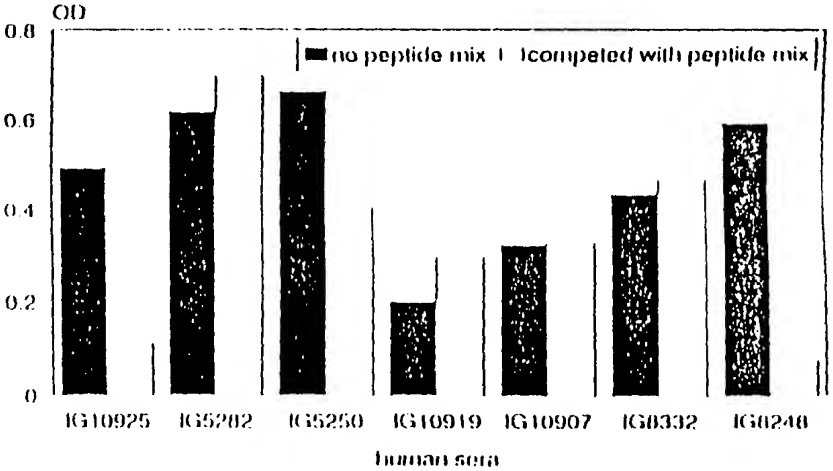
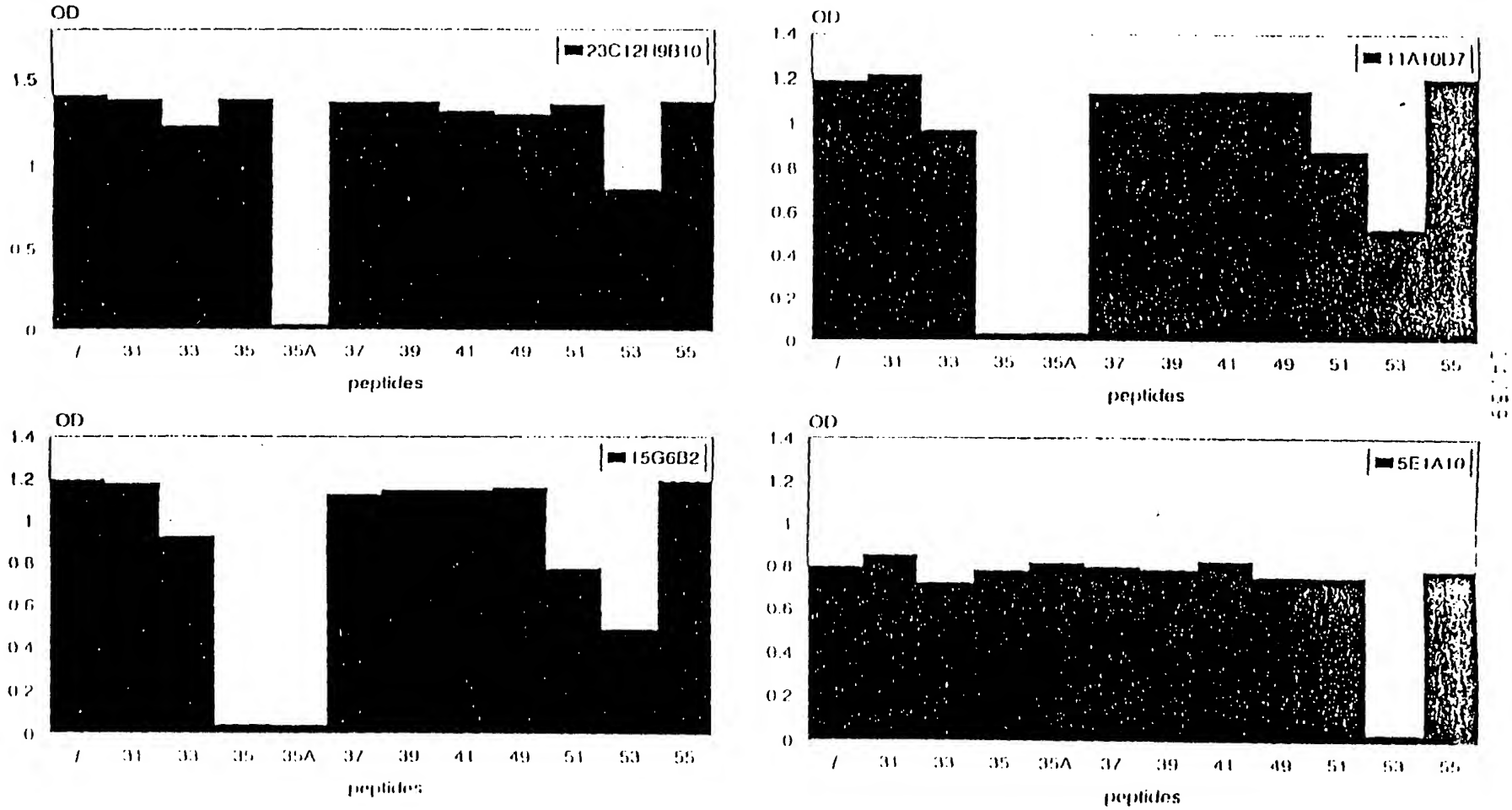
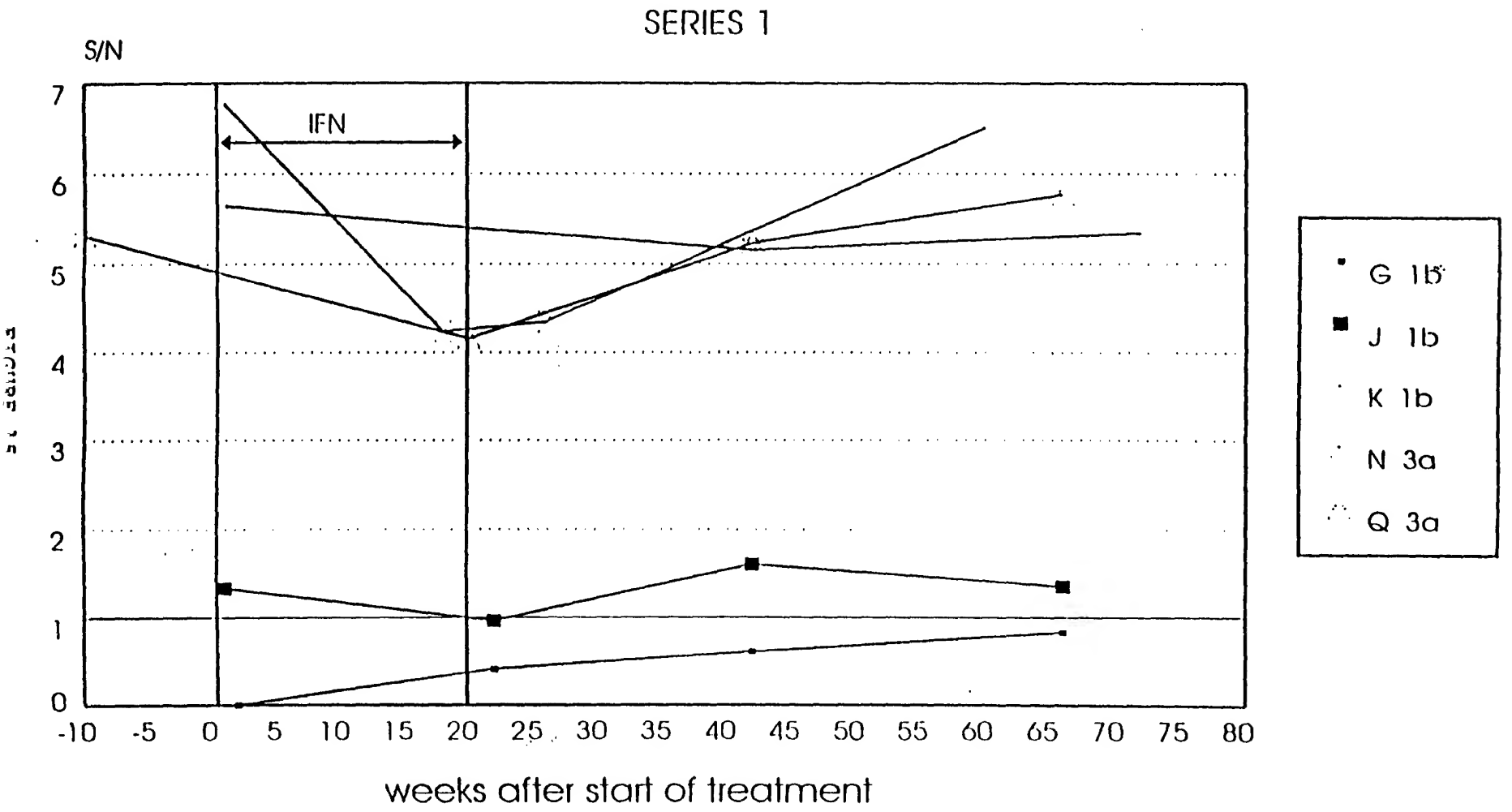


FIGURE 14

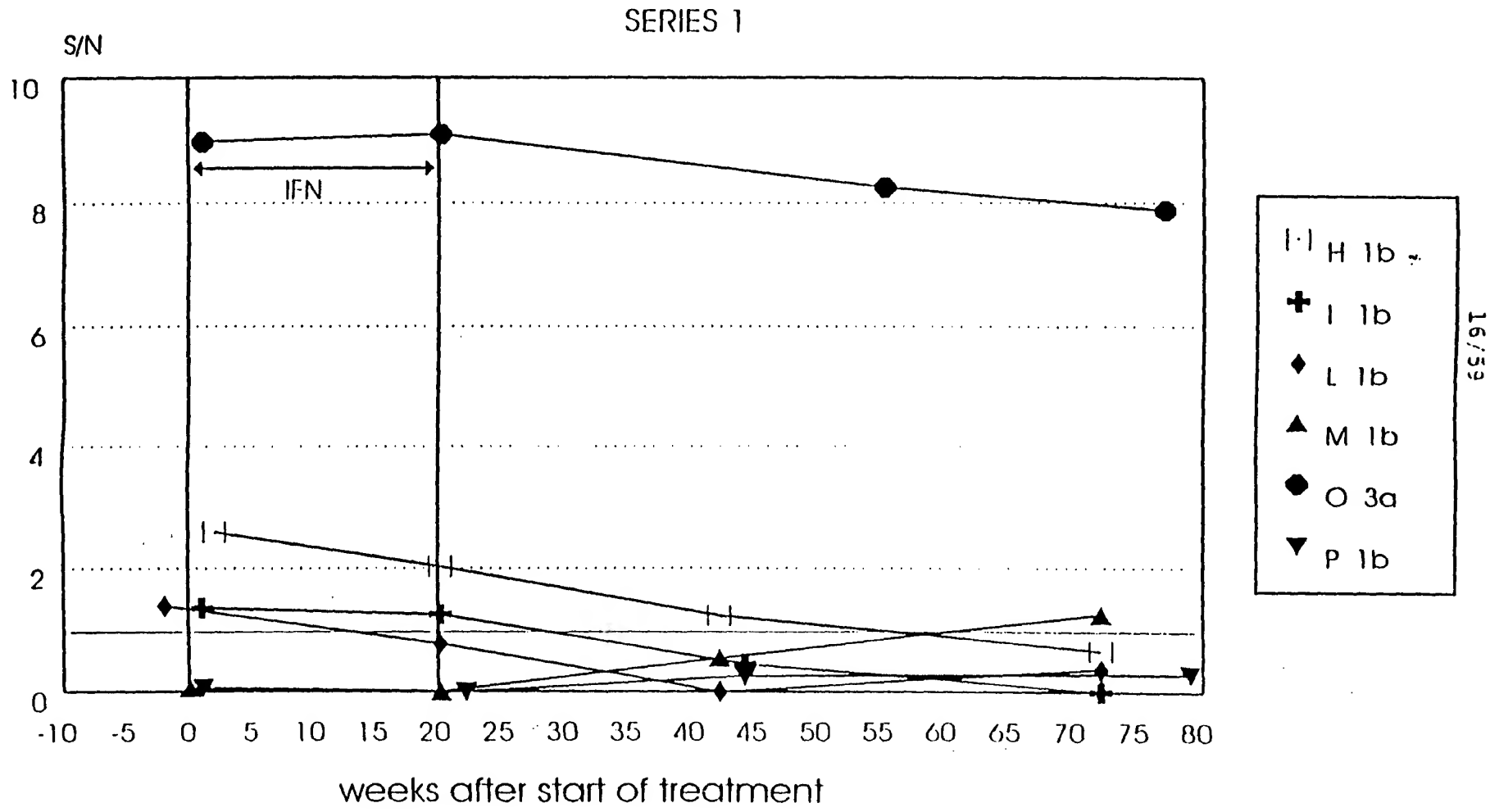
Competition of reactivity of anti-E1 Mabs with peptides



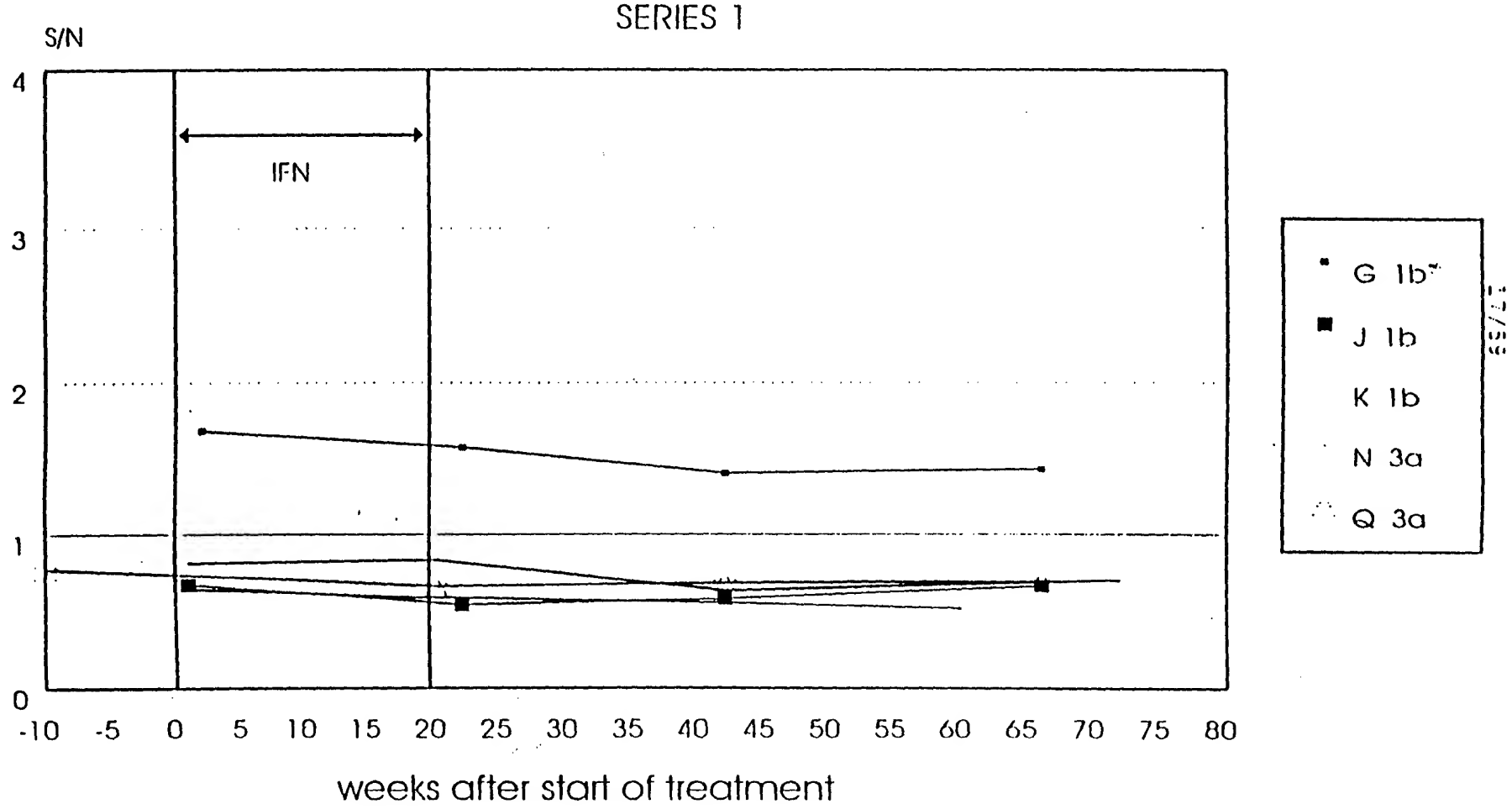
Anti-E1 (epitope 1) levels in NON-RESPONDERS to IFN treatment



Anti-E1 (epitope 1) levels in RESPONDERS to IFN treatment



nti-E1 (epitope 2) levels in NON-RESPONDERS to IFN treatment



Anti-E1 (epitope 2) levels in RESPONDERS to IFN treatment

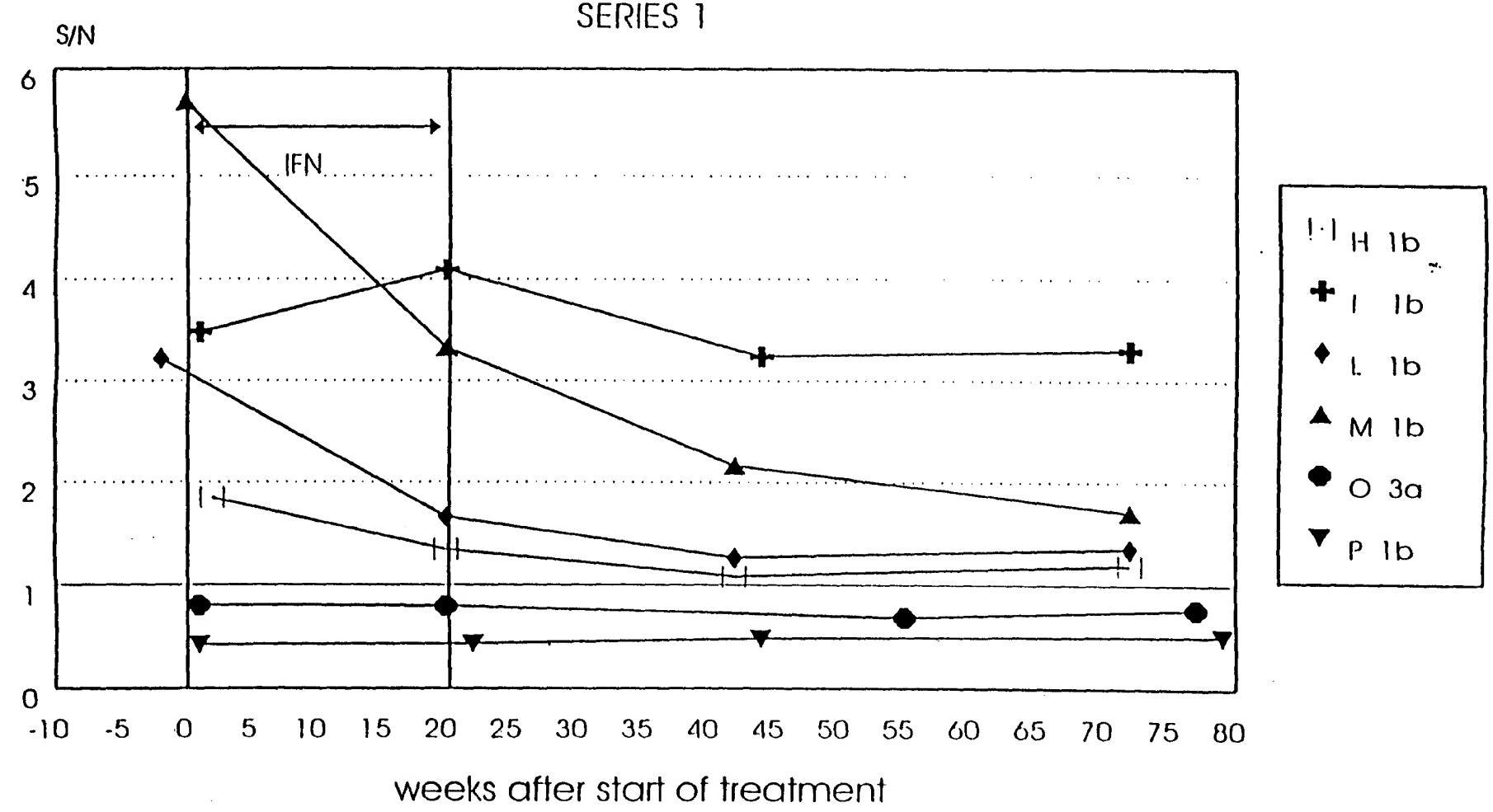


FIGURE 19

Competition of reactivity of anti-E2 Mabs with peptides

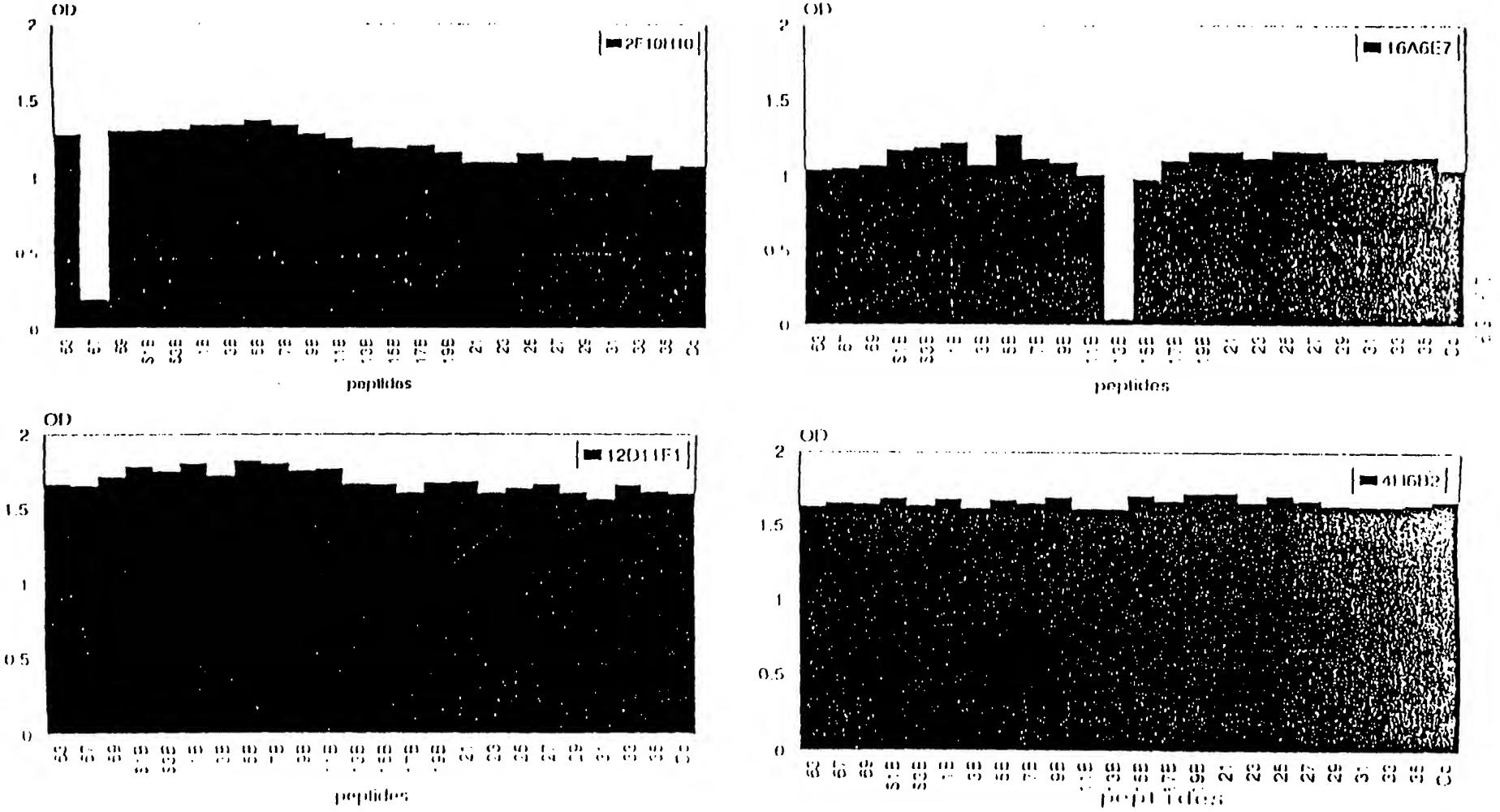


FIGURE 20

Human anti-E2 reactivity competed with peptides

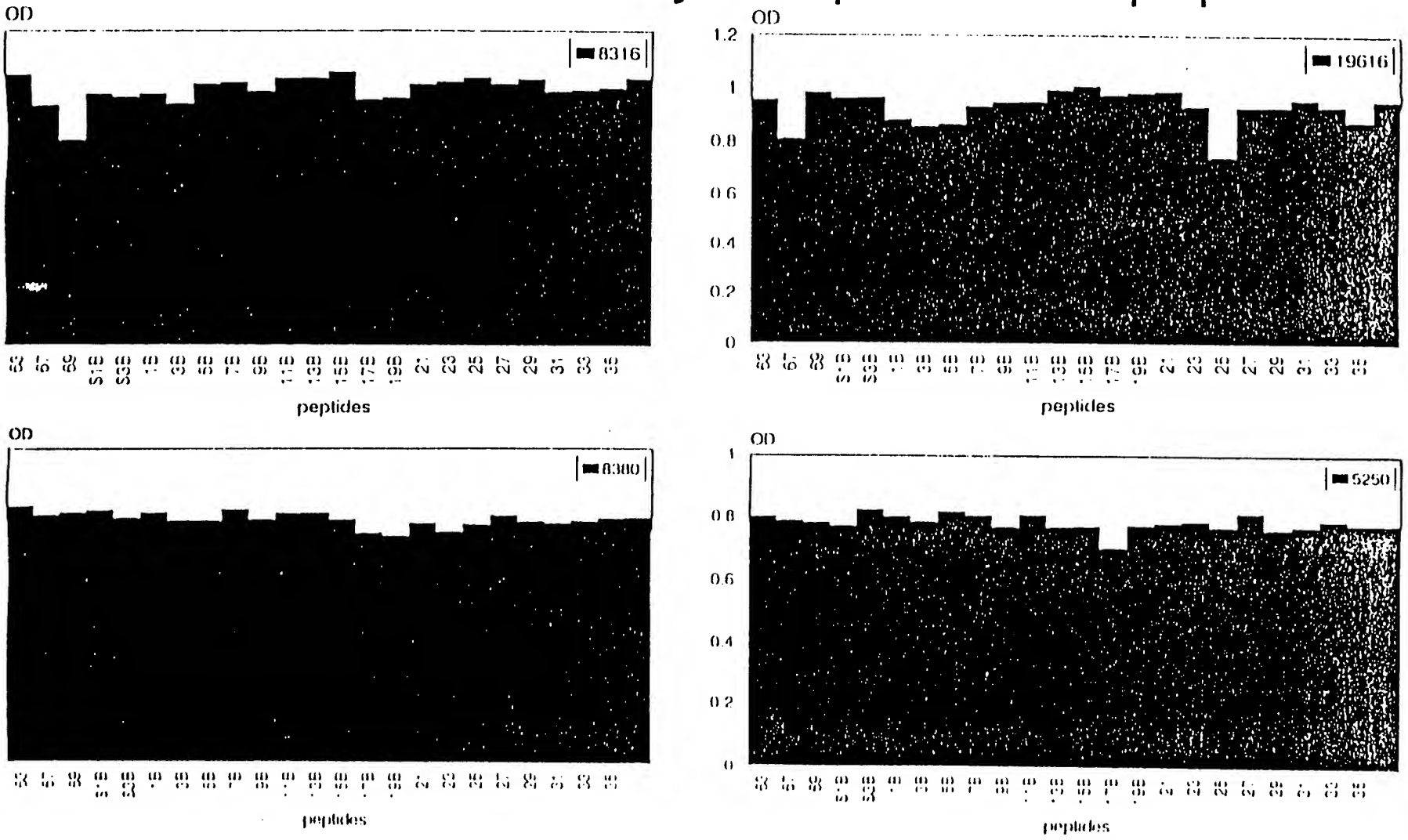


Figure 21

5' GGCATGCAAGCTTAATTAATT3' (SEQ ID NO 1)

3'ACGTCCGTACGTTCGAATTAATTAATCGA5' (SEQ ID NO 94)

5'CCGGGGAGGCCTGCACGTGATCGAGGGCAGACACCATCACCACCATCACTAATAGT TAATTAACTGCA 3' (SEQ ID NO 2)

3'CCTCCGGACGTGCACTAGCTCCCGTCTGTGGTAGTGGTGGTAGTGATTATCAATTAATTG 5' (SEQ ID NO 95)

SEQ ID NO 3 (HCCI9A)

ATGCCCGGTTGCTCTTTCTCTATCTTCCTCTTGGCTTTACTGTCCTGTCTGACCATTCCA
GCTTCCGCTTATGAGGTGCGCAACGTGTCCGGGATGTACCATGTCACGAACGACTGCT
CCAACTCAAGCATTGTGTATGAGGCAGCGGACATGATCATGCACACCCCCGGGTGCGT
GCCCTGCGTTCGGGAGAACAACTCTTCCCGCTGCTGGGTAGCGCTCACCCCCACGCTC
GCAGCTAGGAACGCCAGCGTCCCCACCACGACAATACGACGCCACGTCGATTTGCTCG
TTGGGGCGGCTGCTCTCTGTTCCGCTATGTACGTGGGGGATCTCTGCGGATCTGTCTTC
CTCGTCTCCCAGCTGTTCACCATCTCGCCTCGCCGGCATGAGACGGTGCAGGACTGCA
ATTGCTCAATCTATCCCGGCCACATAACAGGTCACCGTATGGCTTGGGATATGATGAT
GAACTGGTCGCCTACAACGGCCCTGGTGGTATCGCAGCTGCTCCGGATCCCACAAGCT
GTCGTGGACATGGTGGCGGGGGCCCATTGGGGAGTCCTGGCGGGCCTCGCCTACTATT
CCATGGTGGGGAACTGGGCTAAGGTTTTGATTGTGATGCTACTCTTTGCTCTCTAATAG

SEQ ID NO 5 (HCCI10A)

ATGTTGGGTAAGGTCATCGATACCCTTACATGCGGCTTCGCCGACCTCGTGGGGTACA
TTCCGCTCGTCGGCGCCCCCCTAGGGGGCGCTGCCAGGGCCCTGGCGCATGGCGTCCG
GGTTCTGGAGGACGGCGTGAACTATGCAACAGGGAATTTGCCCGGTTGCTCTTTCTCT
ATCTTCCTCTTGGCTTTGCTGTCCTGTCTGACCGTTCCAGCTTCCGCTTATGAAGTGCG
CAACGTGTCCGGGATGTACCATGTCACGAACGACTGCTCCAACTCAAGCATTGTGTAT
GAGGCAGCGGACATGATCATGCACACCCCCGGGTGCGTGCCCTGCGTTCGGGAGAAC
AACTCTTCCCGCTGCTGGGTAGCGCTCACCCCCACGCTCGCAGCTAGGAACGCCAGCG
TCCCCACCACGACAATACGACGCCACGTCGATTTGCTCGTTGGGGCGGCTGCTTTCTG

TTCCGCTATGTACGTGGGGGACCTCTGCGGATCTGTCTTCCTCGTCTCCCAGCTGTTCA
CCATCTCGCCTCGCCGGCATGAGACGGTGCAGGACTGCAATTGCTCAATCTATCCCGG
CCACATAACGGGTCACCGTATGGCTTGGGATATGATGATGAACTGGTCGCCTACAACG
GCCCTGGTGGTATCGCAGCTGCTCCGGATCCCACAAGCTGTCGTGGACATGGTGGCGG
GGGCCCATTGGGGAGTCCTGGCGGGTCTCGCCTACTATTCCATGGTGGGGAACTGGGC
TAAGGTTTTGATTGTGATGCTACTCTTTGCTCCCTAATAG

SEQ ID NO 7 (HCCI11A)

ATGTTGGGTAAGGTCATCGATACCCTTACGTGCGGCTTCGCCGACCTCATGGGGTACA
TTCCGCTCGTCGGCGCCCCCCTAGGGGGTGCTGCCAGAGCCCTGGCGCATGGCGTCCG
GGTTCTGGAAGACGGCGTGAACTATGCAACAGGGAATTTGCCTGGTTGCTCTTTCTCTA
TCTTCCTCTTGGCTTTACTGTCCTGTCTGACCATTCCAGCTTCCGCTTATGAGGTGCGC
AACGTGTCCGGGATGTACCATGTCACGAACGACTGCTCCAACTCAAGCATTGTGTATG
AGGCAGCGGACATGATCATGCACACCCCCGGGTGCGTGCCCTGCGTTCGGGAGAACA
ACTCTTCCCGCTGCTGGGTAGCGCTCACCCCCACGCTCGCAGCTAGGAACGCCAGCGT
CCCCACTACGACAATACGACGCCACGTCGATTTGCTCGTTGGGGCGGCTGCTTTCTGTT
CCGCTATGTACGTGGGGGATCTCTGCGGATCTGTCTTCCTCGTCTCCCAGCTGTTCACC
ATCTCGCCTCGCCGGCATGAGACGGTGCAGGACTGCAATTGCTCAATCTATCCCGGCC
ACATAACAGGTCACCGTATGGCTTGGGATATGATGATGAACTGGTAATAG

SEQ ID NO 9 (HCCI12A)

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GCTTCCGCTTATGAAGTGCGCAACGTGTCCGGGGTGTACCATGTCACGAACGACTGCT
CCAACTCAAGCATAGTGTATGAGGCAGCGGACATGATCATGCACACCCCCGGGTGCGT
GCCCTGCGTTCGGGAGGGCAACTCCTCCCGTTGCTGGGTGGCGCTCACTCCCACGCTC
GCGGCCAGGAACGCCAGCGTCCCCACAACGACAATACGACGCCACGTCGATTTGCTC
GTTGGGGCTGCTGCTTTCTGTTCCGCTATGTACGTGGGGGATCTCTGCGGATCTGTTTT
CCTTGTTTCCCAGCTGTTCACCTTCTCACCTCGCCGGCATCAAACAGTACAGGACTGCA
ACTGCTCAATCTATCCCGGCCATGTATCAGGTCACCGCATGGCTTGGGATATGATGAT
GAACTGGTCCTAATAG

SEQ ID NO 11 (HCCI13A)

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GCTTCCGCTTATGAAGTGCGCAACGTGTCCGGGGTGTACCATGTCACGAACGACTGCT
CCAACTCAAGCATAGTGTATGAGGCAGCGGACATGATCATGCACACCCCCGGGTGCGT

GCCCTGCGTTCGGGAGGGCAACTCCTCCCGTTGCTGGGTGGCGCTCACTCCCACGCTC
GCGGCCAGGAACGCCAGCGTCCCCACAACGACAATACGACGCCACGTCGATTTGCTC
GTTGGGGCTGCTGCTTTCTGTTCCGCTATGTACGTGGGGGATCTCTGCGGATCTGTTTT
CCTTGTTTCCCAGCTGTTCACCTTCTCACCTCGCCGGCATCAAACAGTACAGGACTGCA
ACTGCTCAATCTATCCCGGCCATGTATCAGGTCACCGCATGGCTTGGGATATGATGAT
GAACTGGTAATAG

SEQ ID NO 13 (HCCI17A)
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TTCCGCTCGTCGGCGCCCCCCTAGGGGGCGCTGCCAGGGCCCTGGCGCATGGCGTCCG
GGTTCTGGAAGACGGCGTGAACTATGCAACAGGGAATTTGCCTGGTTGCTCTTTCTCTA
TCTTCCTCTTGGCTTTACTGTCCTGTCTAACCATTCCAGCTTCCGCTTACGAGGTGCGC
AACGTGTCCGGGATGTACCATGTCACGAACGACTGCTCCAACTCAAGCATTGTGTATG
AGGCAGCGGACATGATCATGCACACCCCCGGGTGCGTGCCCTGCGTTCGGGAGAACA
ACTCTTCCCGCTGCTGGGTAGCGCTCACCCCCACGCTCGCGGCTAGGAACGCCAGCAT
CCCCACTACAACAATACGACGCCACGTCGATTTGCTCGTTGGGGCGGCTGCTTTCTGTT
CCGCTATGTACGTGGGGGATCTCTGCGGATCTGTCTTCCTCGTCTCCCAGCTGTTCACC
ATCTCGCCTCGCCGGCATGAGACGGTGCAGGACTGCAATTGCTCAATCTATCCCGGCC
ACATAACGGGTCACCGTATGGCTTGGGATATGATGATGAACTGGTACTAATAG

SEQ ID NO 15 (HCPr51)
ATGCCCGGTTGCTCTTTCTCTATCTT

SEQ ID NO 16 (HCPr52)
ATGTTGGGTAAGGTCATCGATACCCT

SEQ ID NO 17 (HCPr53)
CTATTAGGACCAGTTCATCATCATATCCCA

SEQ ID NO 18 (HCPr54)
CTATTACCAGTTCATCATCATATCCCA

SEQ ID NO 19 (HCPr107)
ATACGACGCCACGTCGATTCCCAGCTGTTCACCATC

SEQ ID NO 20 (HCPr108)

GATGGTGAACAGCTGGGAATCGACGTGGCGTCGTAT

SEQ ID NO 21 (HCCI37)

ATGTTGGGTAAGGTCATCGATACCCTTACATGCGGCTTCGCCGACCTCGTGGGGTACA
TTCCGCTCGTCGGCGCCCCCCTAGGGGGCGCTGCCAGGGCCCTGGCGCATGGCGTCCG
GGTTCTGGAGGACGGCGTGAACTATGCAACAGGGAATTTGCCCGGTTGCTCTTTCTCT
ATCTTCCTCTTGGCTTTGCTGTCCTGTCTGACCGTTCCAGCTTCCGCTTATGAAGTGCG
CAACGTGTCCGGGATGTACCATGTCACGAACGACTGCTCCAACTCAAGCATTGTGTAT
GAGGCAGCGGACATGATCATGCACACCCCCGGGTGCGTGCCCTGCGTTCGGGAGAAC
AACTCTTCCCGCTGCTGGGTAGCGCTCACCCCCACGCTCGCAGCTAGGAACGCCAGCG
TCCCCACCACGACAATACGACGCCACGTCGATTCCCAGCTGTTCACCATCTCGCCTCG
CCGGCATGAGACGGTGCAGGACTGCAATTGCTCAATCTATCCCGGCCACATAACGGGT
CACCGTATGGCTTGGGATATGATGATGAACTGGTCGCCTACAACGGCCCTGGTGGTAT
CGCAGCTGCTCCGGATCCCACAAGCTGTCGTGGACATGGTGGCGGGGGCCCATTGGGG
AGTCCTGGCGGGTCTCGCCTACTATTCCATGGTGGGGAACTGGGCTAAGGTTTTGATTG
TGATGCTACTCTTTGCTCCCTAATAG

SEQ ID NO 23 (HCCI38)

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ATCTTCCTCTTGGCTTTGCTGTCCTGTCTGACCGTTCCAGCTTCCGCTTATGAAGTGCG
CAACGTGTCCGGGATGTACCATGTCACGAACGACTGCTCCAACTCAAGCATTGTGTAT
GAGGCAGCGGACATGATCATGCACACCCCCGGGTGCGTGCCCTGCGTTCGGGAGAAC
AACTCTTCCCGCTGCTGGGTAGCGCTCACCCCCACGCTCGCAGCTAGGAACGCCAGCG
TCCCCACCACGACAATACGACGCCACGTCGATTCCCAGCTGTTCACCATCTCGCCTCG
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CACCGTATGGCTTGGGATATGATGATGAACTGGTAA
TAG

SEQ ID NO 25 (HCCI39)

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GGTTCTGGAGGACGGCGTGAACTATGCAACAGGGAATTTGCCCGGTTGCTCTTTCTCT

ATCTTCCTCTTGGCTTTGCTGTCCTGTCTGACCGTTCCAGCTTCCGCTTATGAAGTGCG
CAACGTGTCCGGGATGTACCATGTCACGAACGACTGCTCCAACTCAAGCATTGTGTAT
GAGGCAGCGGACATGATCATGCACACCCCCGGGTGCGTGCCCTGCGTTCGGGAGAAC
AACTCTTCCCGCTGCTGGGTAGCGCTCACCCCCACGCTCGCAGCTAGGAACGCCAGCG
TCCCCACCACGACAATACGACGCCACGTCGATTCCCAGCTGTTCACCATCTCGCCTCG
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CGCAGCTGCTCCGGATCCTCTAATAG

SEQ ID NO 27 (HCCI40)

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CAACGTGTCCGGGATGTACCATGTCACGAACGACTGCTCCAACTCAAGCATTGTGTAT
GAGGCAGCGGACATGATCATGCACACCCCCGGGTGCGTGCCCTGCGTTCGGGAGAAC
AACTCTTCCCGCTGCTGGGTAGCGCTCACCCCCACGCTCGCAGCTAGGAACGCCAGCG
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SEQ ID NO 29 (HCCI62)

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CCTTGAAGACGGGATAAATTTCGCAACAGGGAATTTGCCCGGTTGCTCCTTTTCTATTT
TCCTTCTCGCTCTGTTCTCTTGCTTAATTCATCCAGCAGCTAGTCTAGAGTGGCGGAAT
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CGATGACGTTATTCTGCACACACCCGGCTGCATACCTTGTGTCCAGGACGGCAATACA
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CCGCTTCGATACGCAGTCATGTGGACCTATTAGTGGGCGCGGCCACGATGTGCTCTGC
GCTCTACGTGGGTGACATGTGTGGGGCTGTCTTCCTCGTGGGACAAGCCTTCACGTTCA
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SEQ ID NO 31 (HCCl63)

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CCTTGAGGACGGGGTAAACTATGCAACAGGGAATTTACCCGGTTGCTCTTTCTCTATCT
TTATTCTTGCTCTTCTCTCGTGTCTGACCGTTCCGGCCTCTGCAGTTCCCTACCGAAATG
CCTCTGGGATTTATCATGTTACCAATGATTGCCCAAACTCTTCCATAGTCTATGAGGCA
GATAACCTGATCCTACACGCACCTGGTTGCGTGCCTTGTGTCATGACAGGTAATGTGA
GTAGATGCTGGGTCCAAATTACCCCTACACTGTCAGCCCCGAGCCTCGGAGCAGTCAC
GGCTCCTCTTCGGAGAGCCGTTGACTACCTAGCGGGAGGGGCTGCCCTCTGCTCCGCG
TTATACGTAGGAGACGCGTGTGGGGCACTATTCTTGGTAGGCCAAATGTTCACCTATA
GGCCTCGCCAGCACGCTACGGTGCAGAACTGCAACTGTTCCATTTACAGTGGCCATGT
TACCGGCCACCGGATGGCATGGGATATGATGATGAACTGGTAATAG

SEQ ID NO 33 (HCPr109)

TGGGATATGATGATGAACTGGTC

SEQ ID NO 34 (HCPr72)

CTATTATGGTGGTAAKGCCARCARGAGCAGGAG

SEQ ID NO 35 (HCCL22A)

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GCCTCGCCTACTATTCCATGGTGGGGAACTGGGCTAAGGTTTTGGTTGTGATGCTACTC
TTTGCCGGCGTCGACGGGCATACCCGCGTGTCAGGAGGGGCAGCAGCCTCCGATACCA
GGGGCCTTGTGTCCCTCTTTAGCCCCGGGTCGGCTCAGAAAATCCAGCTCGTAAACAC
CAACGGCAGTTGGCACATCAACAGGACTGCCCTGAACTGCAACGACTCCCTCCAAAC
AGGGTTCTTTGCCGCACTATTCTACAAACACAAATTCAACTCGTCTGGATGCCCAGAG
CGCTTGGCCAGCTGTCGCTCCATCGACAAGTTCGCTCAGGGGTGGGGTCCCCTCACTT
ACACTGAGCCTAACAGCTCGGACCAGAGGCCCTACTGCTGGCACTACGCGCCTCGACC
GTGTGGTATTGTACCCGCGTCTCAGGTGTGCGGTCCAGTGTATTGCTTCACCCCGAGCC
CTGTTGTGGTGGGGACGACCGATCGGTTTGGTGTCCCCACGTATAACTGGGGGGCGAA
CGACTCGGATGTGCTGATTCTCAACAACACGCGGCCGCCGCGAGGCAACTGGTTCGGC
TGTACATGGATGAATGGCACTGGGTTCACCAAGACGTGTGGGGGCCCCCCGTGCAACA
TCGGGGGGGCCGGCAACAACACCTTGACCTGCCCCACTGACTGTTTTCGGAAGCACCC
CGAGGCCACCTACGCCAGATGCGGTTCTGGGCCCTGGCTGACACCTAGGTGTATGGTT

CATTACCCATATAGGCTCTGGCACTACCCCTGCACTGTCAACTTCACCATCTTCAAGGT
TAGGATGTACGTGGGGGGCGTGGAGCACAGGTTCGAAGCCGCATGCAATTGGACTCG
AGGAGAGCGTTGTGACTTGGAGGACAGGGATAGATCAGAGCTTAGCCCGCTGCTGCTG
TCTACAACAGAGTGGCAGATACTGCCCTGTTCCTTCACCACCCTGCCGGCCCTATCCA
CCGGCCTGATCCACCTCCATCAGAACATCGTGGACGTGCAATACCTGTACGGTGTAGG
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SEQ ID NO 37 (HCCI41)

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CGCTTGGCCAGCTGTCGCTCCATCGACAAGTTCGCTCAGGGGTGGGGTCCCCTCACTT
ACACTGAGCCTAACAGCTCGGACCAGAGGCCCTACTGCTGGCACTACGCGCCTCGACC
GTGTGGTATTGTACCCGCGTCTCAGGTGTGCGGTCCAGTGTATTGCTTCACCCCGAGCC
CTGTTGTGGTGGGGACGACCGATCGGTTTGGTGTCCCCACGTATAACTGGGGGGCGAA
CGACTCGGATGTGCTGATTCTCAACAACACGCGGCCGCCGCGAGGCAACTGGTTCGGC
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CATTACCCATATAGGCTCTGGCACTACCCCTGCACTGTCAACTTCACCATCTTCAAGGT
TAGGATGTACGTGGGGGGCGTGGAGCACAGGTTCGAAGCCGCATGCAATTGGACTCG
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SEQ ID NO 39 (HCCI42)

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CCTCGCCTACTATTCCATGGTGGGGAACTGGGCTAAGGTTTTGGTTGTGATGCTACTCT

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GGGGCCTTGTGTCCCTCTTTAGCCCCGGGTCGGCTCAGAAAATCCAGCTCGTAAACAC
CAACGGCAGTTGGCACATCAACAGGACTGCCCTGAACTGCAACGACTCCCTCCAAAC
AGGGTTCTTTGCCGCACTATTCTACAAACACAAATTCAACTCGTCTGGATGCCCAGAG
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CGACTCGGATGTGCTGATTCTCAACAACACGCGGCCGCCGCGAGGCAACTGGTTCGGC
TGTACATGGATGAATGGCACTGGGTTCACCAAGACGTGTGGGGGCCCCCCGTGCAACA
TCGGGGGGGCCGGCAACAACACCTTGACCTGCCCCACTGACTGTTTTCGGAAGCACCC
CGAGGCCACCTACGCCAGATGCGGTTCTGGGCCCTGGCTGACACCTAGGTGTATGGTT
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SEQ ID NO 41 (HCCI43)

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TATTCTACAAACACAAATTCAACTCGTCTGGATGCCCAGAGCGCTTGGCCAGCTGTCG
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CGTCTCAGGTGTGCGGTCCAGTGTATTGCTTCACCCCGAGCCCTGTTGTGGTGGGGAC
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CAGAGCTTAATTAATTAG

SEQ ID NO 43 (HCCl44)

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SEQ ID NO 45 (HCCL64)

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SEQ ID NO 47 (HCCI65)

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CCAGTGTATTGCTTCACCCCGAGCCCTGTTGTGGTGGGGACGACCGATCGGTTTGGTGT
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SEQ ID NO 49 (HCCI66)

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TGTGGCCGCTGCTCCTGCTTCTGCTGGCCTTACCACCACGAGCTTATGCCTAGTAA

Figure 22

OD measured at 450 nm

Fraction	volume	dilution	construct 39 Type 1b	40 Type 1b	62 Type 3a	63 Type 3a
START	23 ml	1/20	2.517	1.954	1.426	1.142
FLOW THROUGH	23 ml	1/20	0.087	0.085	0.176	0.120
1	0.4 ml	1/200	0.102	0.051	0.048	0.050
2			0.396	0.550	0.090	0.067
3			2.627	2.603	2.481	2.372
4			3	2.967	3	2.694
5			3	2.810	2.640	2.154
6			2.694	2.499	1.359	1.561
7			2.408	2.481	0.347	1.390
8			2.176	1.970	1.624	0.865
9			1.461	1.422	0.887	0.604
10			1.286	0.926	0.543	0.519
11			0.981	0.781	0.294	0.294
12			0.812	0.650	0.249	0.199
13			0.373	0.432	0.239	0.209
14			0.653	0.371	0.145	0.184
15			0.441	0.348	0.151	0.151
16			0.321	0.374	0.098	0.106
17			0.525	0.186	0.099	0.108
18			0.351	0.171	0.083	0.090
19			0.192	0.164	0.084	0.087

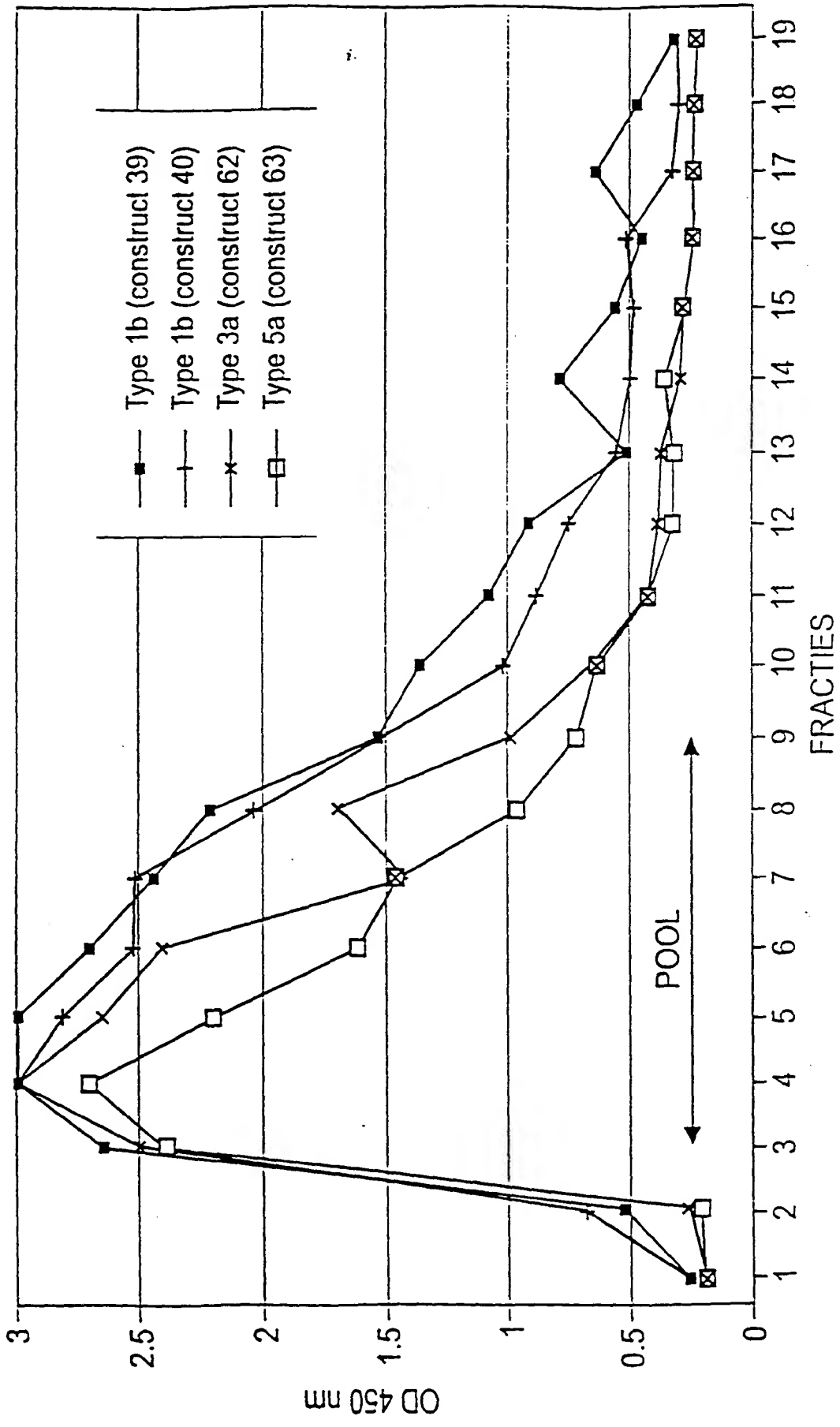

Type 1b (construct 39)
Type 1b (construct 40)
Type 3a (construct 62)
Type 5a (construct 63)
POOL
FRACTIES
OD 450 nm
0
0.5
1
1.5
2
2.5
3
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19

 Figure 24

Fraction	volume	dilution	OD measured at 450 nm construct 39 Type 1b	40 Type 1b	62 Type 3a	63 Type 5a
20	250 µl	1/200	0.072	0.130	0.096	0.051
21			0.109	0.293	0.084	0.052
22			0.279	0.249	0.172	0.052
23			0.093	0.151	0.297	0.054
24			0.080	0.266	0.438	0.056
25			0.251	0.100	0.457	0.048
26			3	1.649	0.722	0.066
27			3	3	2.528	0.889
28			3	3	3	2.345
29			3	3	2.849	2.580
30			2.227	1.921	1.424	1.333
31			0.263	0.415	0.356	0.162
32			0.071	0.172	0.154	0.064
33			0.103	0.054	0.096	0.057
34			0.045	0.045	0.044	0.051
35			0.043	0.047	0.045	0.046
36			0.045	0.045	0.049	0.040
37			0.045	0.047	0.046	0.048
38			0.046	0.048	0.047	0.057
39			0.045	0.048	0.050	0.057
40			0.046	0.049	0.048	0.049

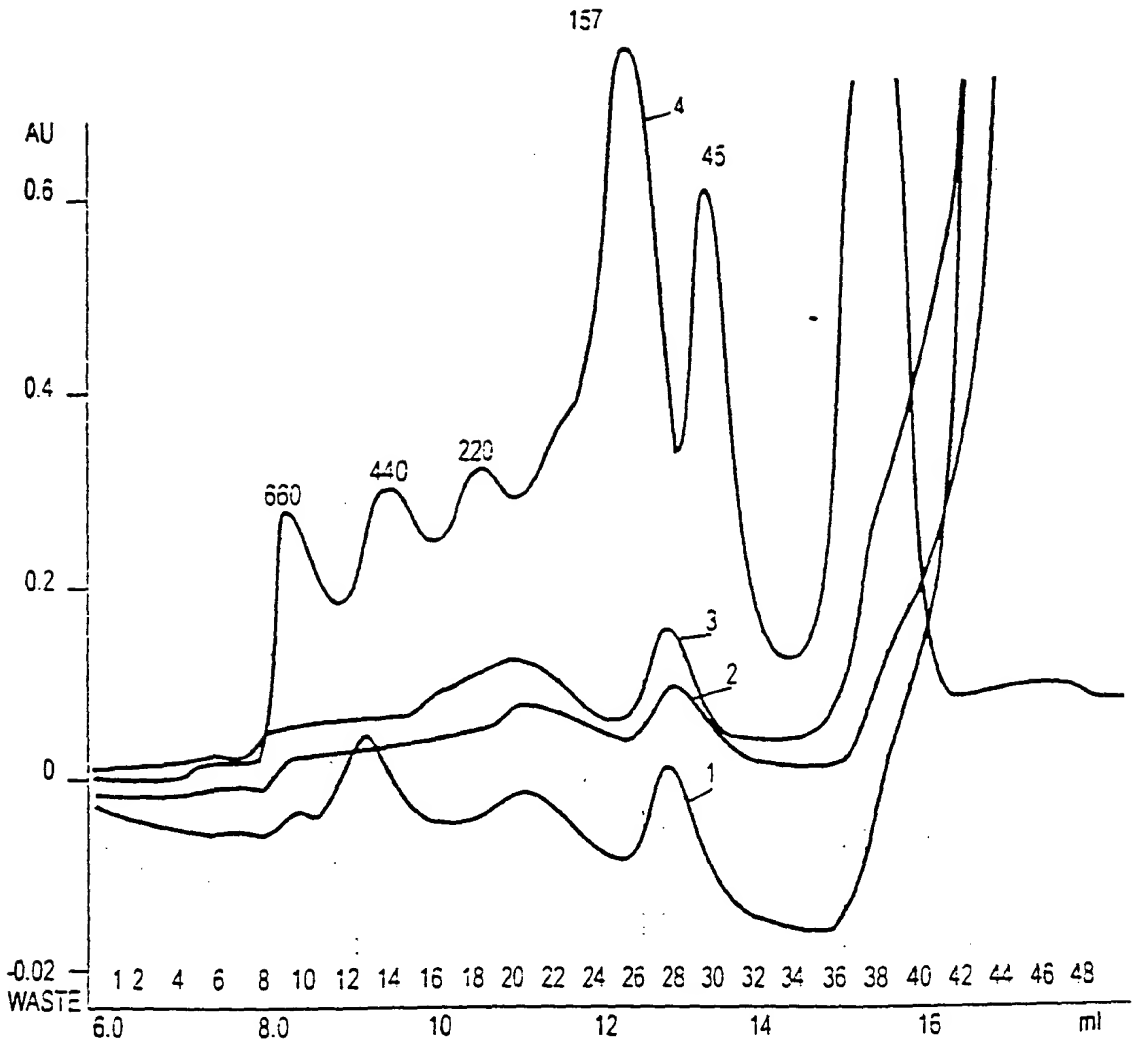

157
AU
0.6
0.4
0.2
0
-0.02
WASTE
660
440
220
4
45
3
2
1
1 2 4 6 8 10 12 14 16 18 20 22 24 26 28 30 32 34 36 38 40 42 44 46 48
6.0
8.0
10
12
14
16
ml

FIGURE 25

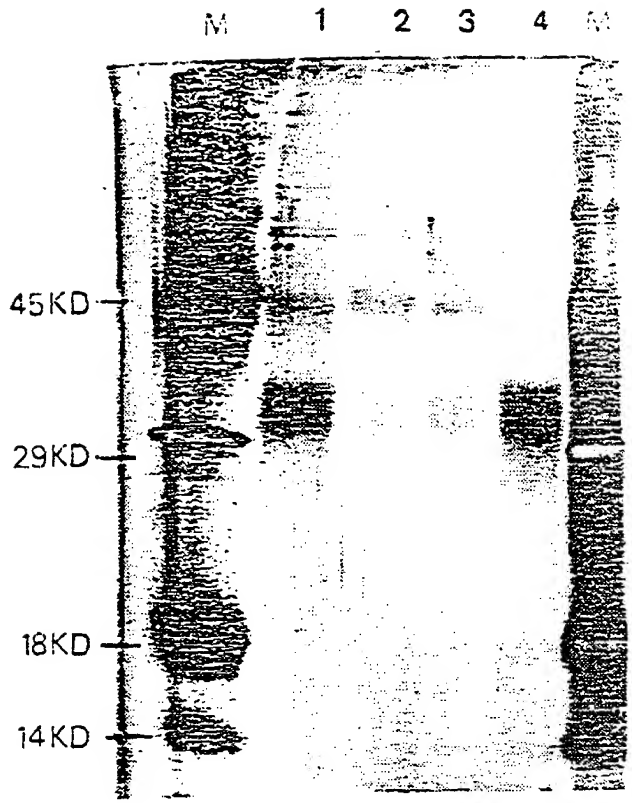


Figure 26

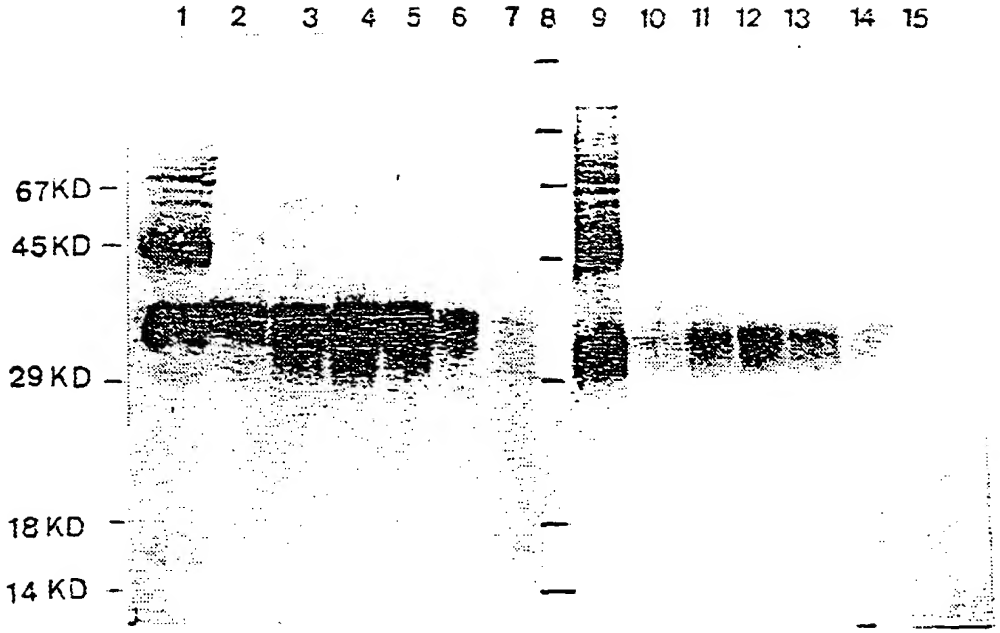


Figure 27

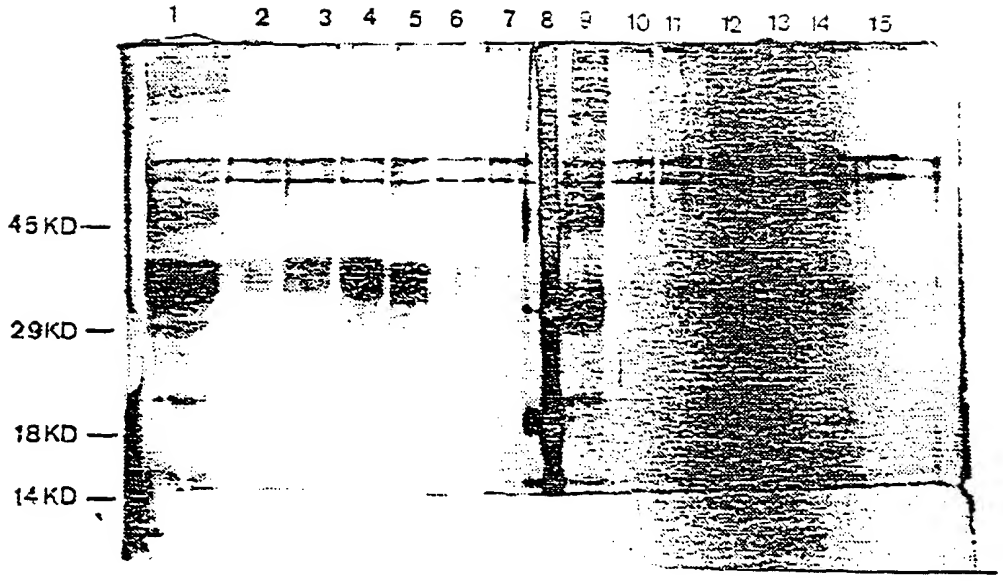
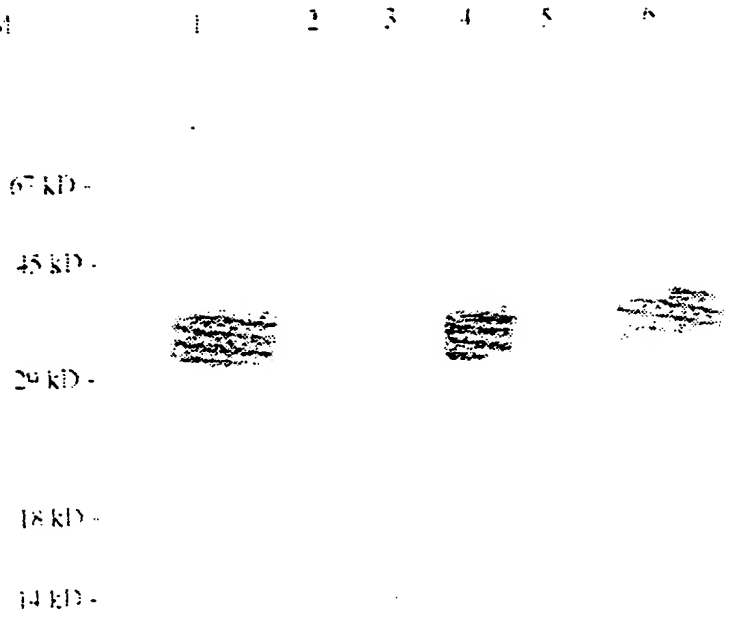


Figure 28



Lane 1: Crude Lysate
Lane 2: Flow through Lentil Chromatography
Lane 3: Wash with EMPIGEN Lentil Chromatography
Lane 4: Eluate Lentil Chromatography
Lane 5: Flow through during concentration lentil eluate
Lane 6: Pool of Eluate after Size Exclusion Chromatography

Figure 29: Western Blot Analysis with anti-E1 mouse monoclonal 5E1A10

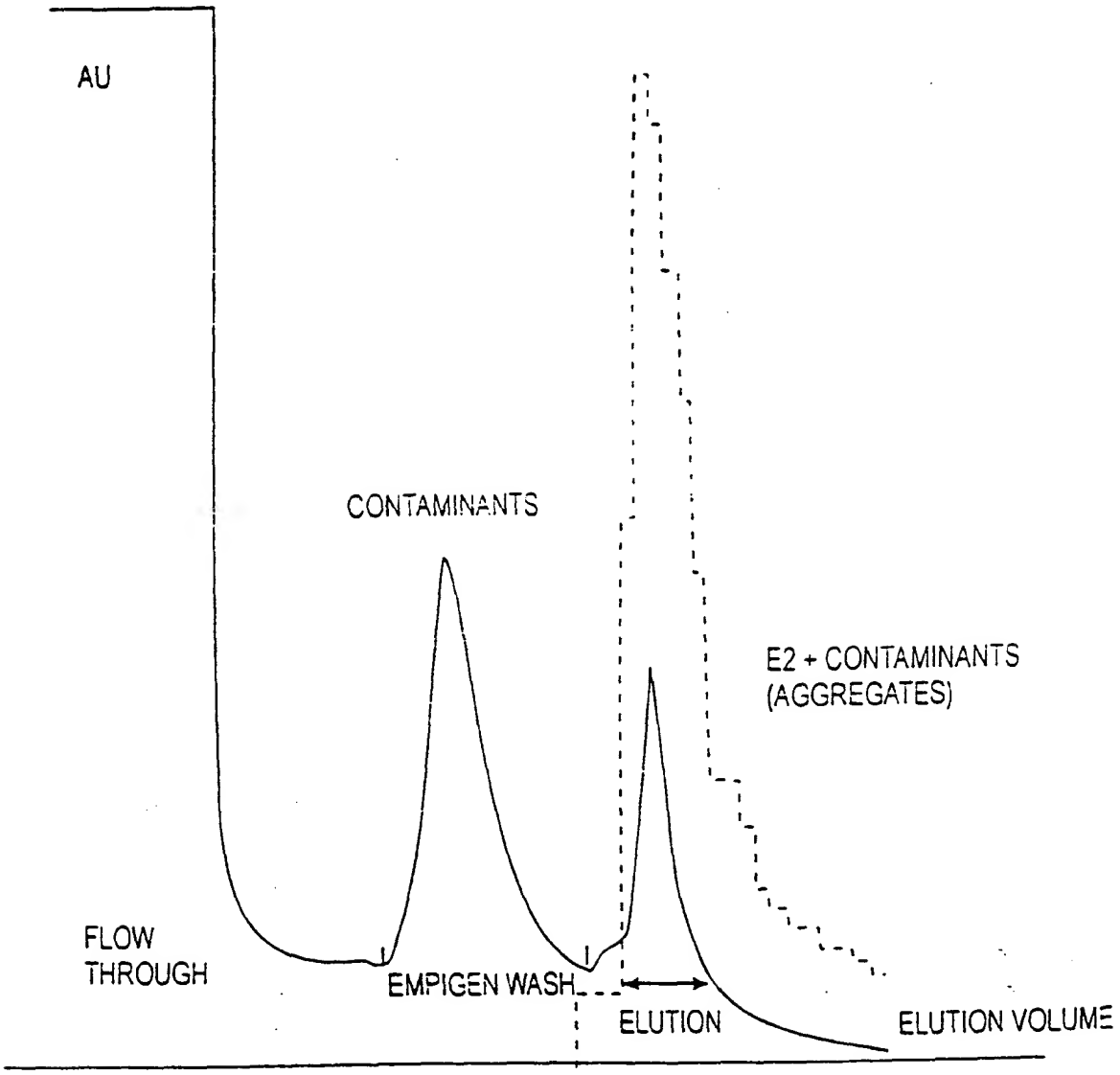
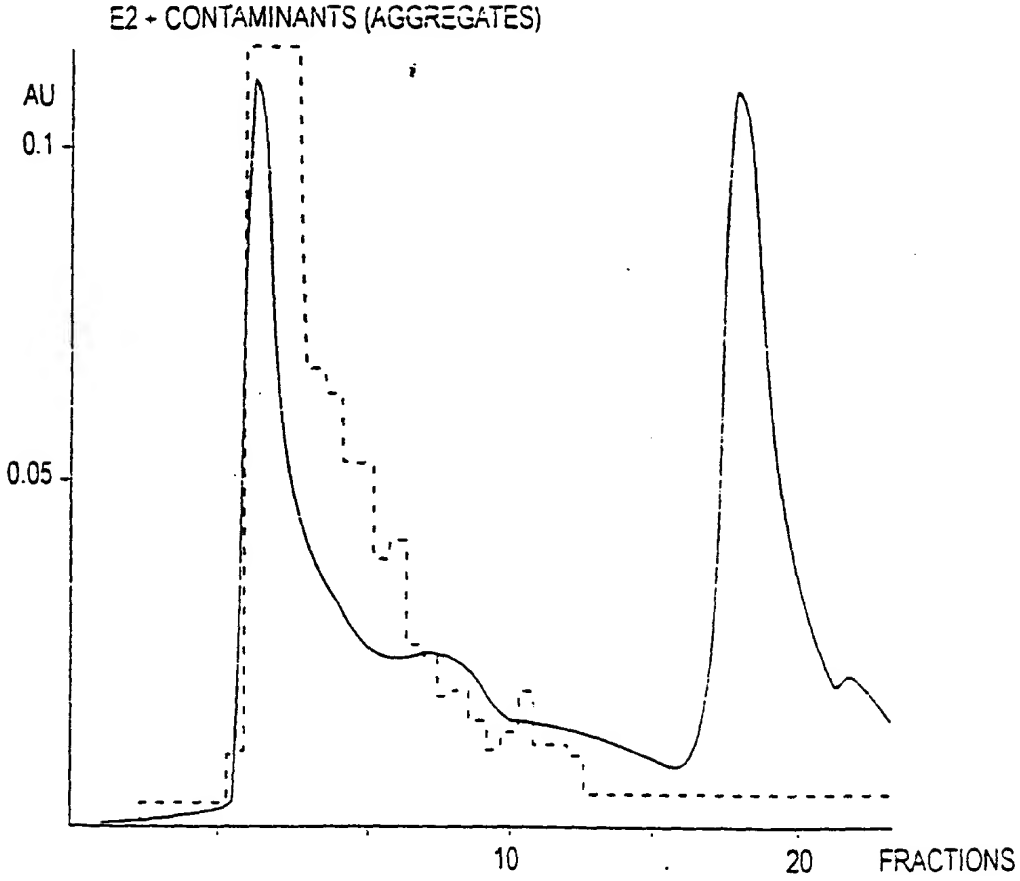

AU
CONTAMINANTS
E2 + CONTAMINANTS
(AGGREGATES)
FLOW
THROUGH
EMPIGEN WASH
ELUTION
ELUTION VOLUME

FIGURE 30

A: NON - REDUCED



B : REDUCED

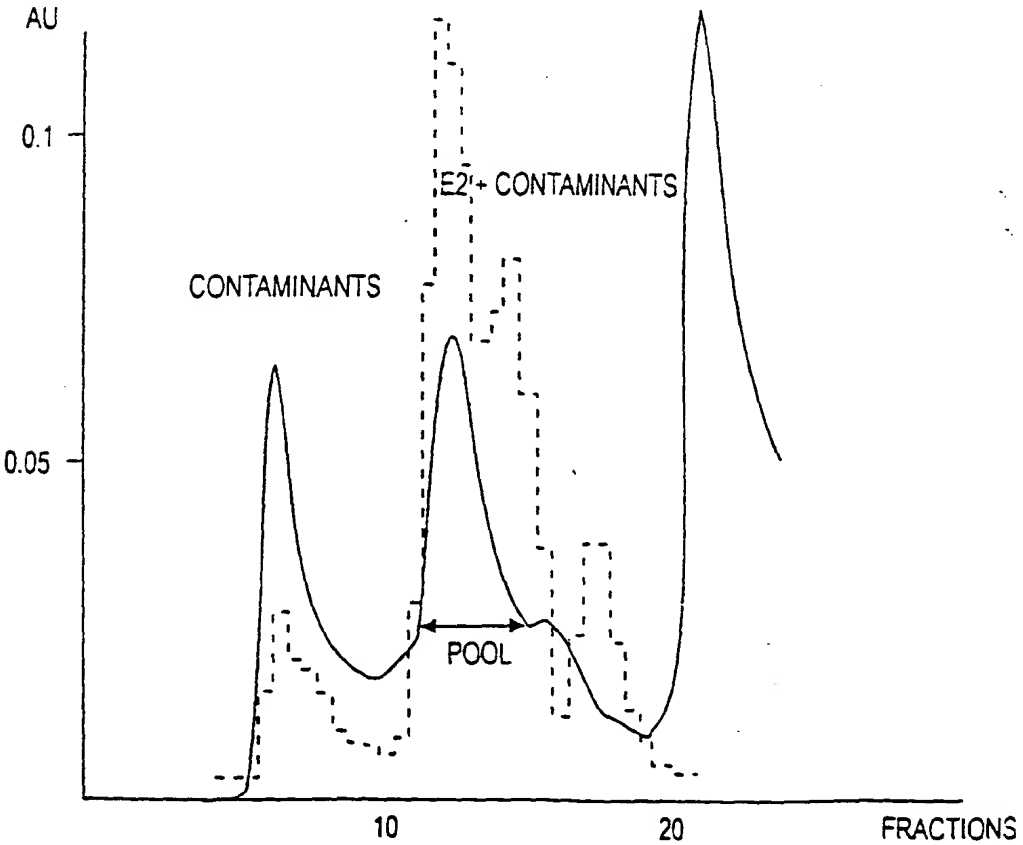


FIGURE 21

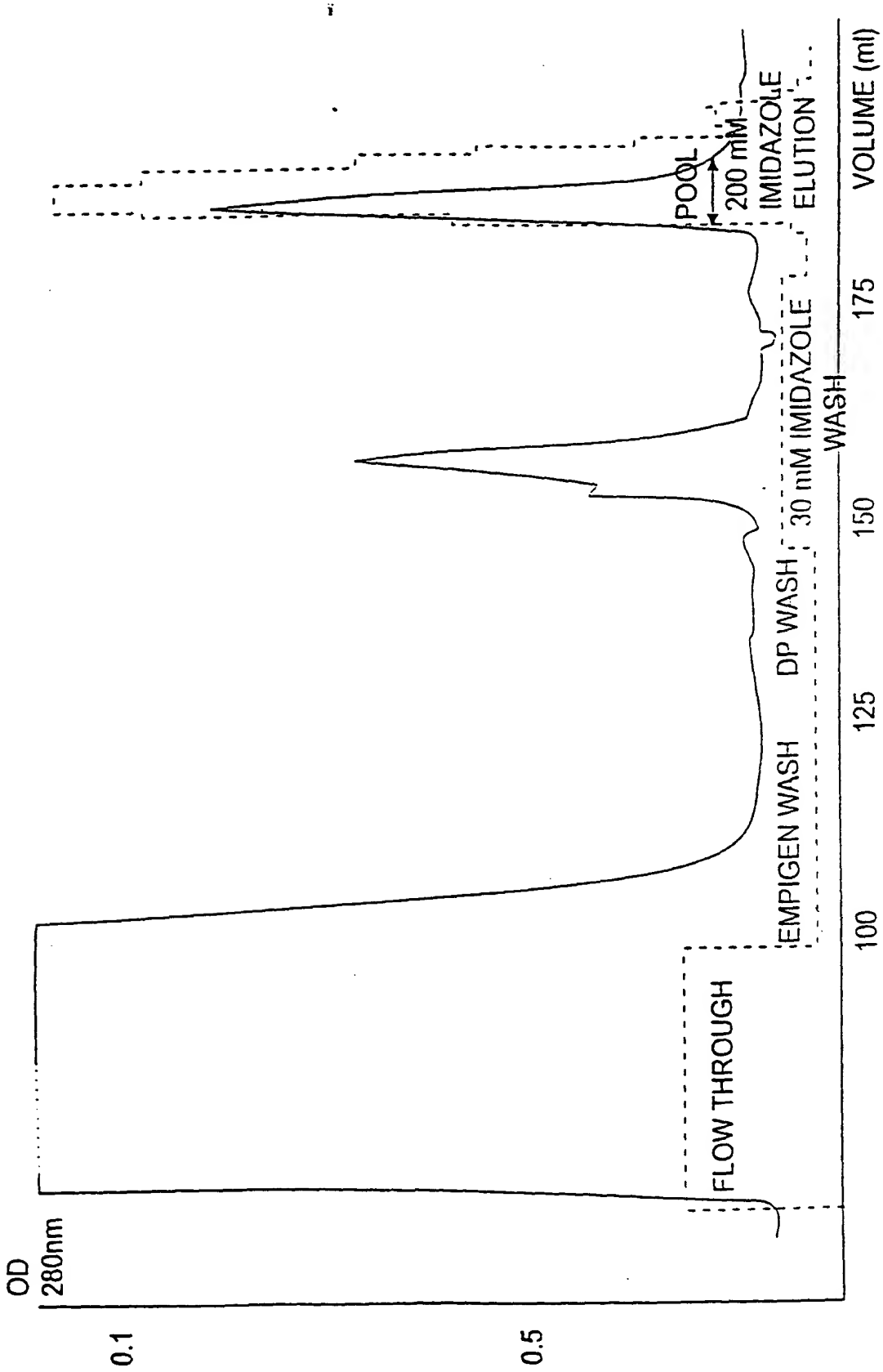
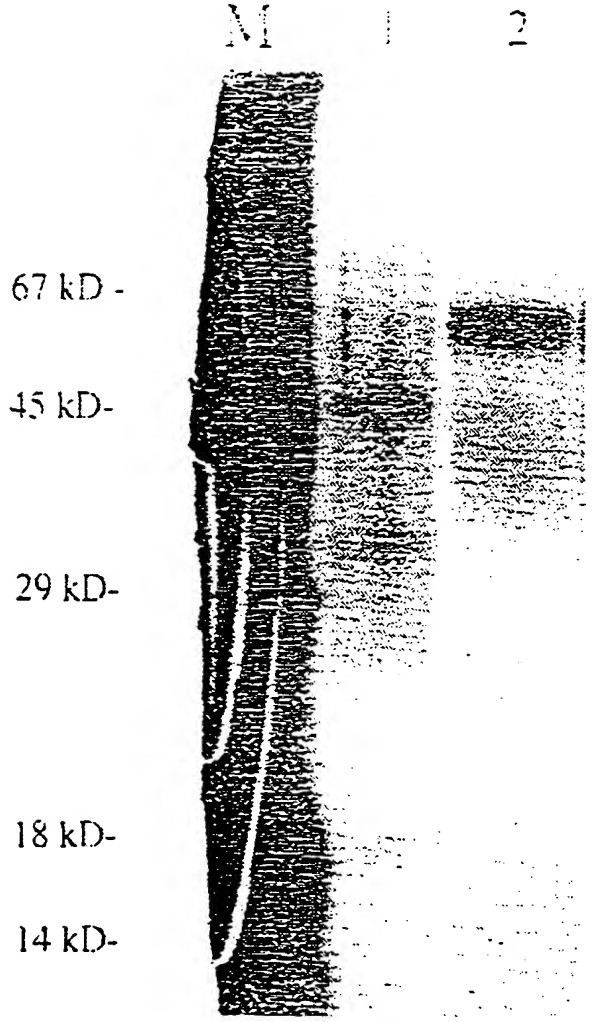

OD
280nm
0.1
0.5
FLOW THROUGH
EMPIGEN WASH
DP WASH
30 mM IMIDAZOLE
WASH
IMIDAZOLE
ELUTION
200 mM
POOL
100
125
150
175
VOLUME (ml)

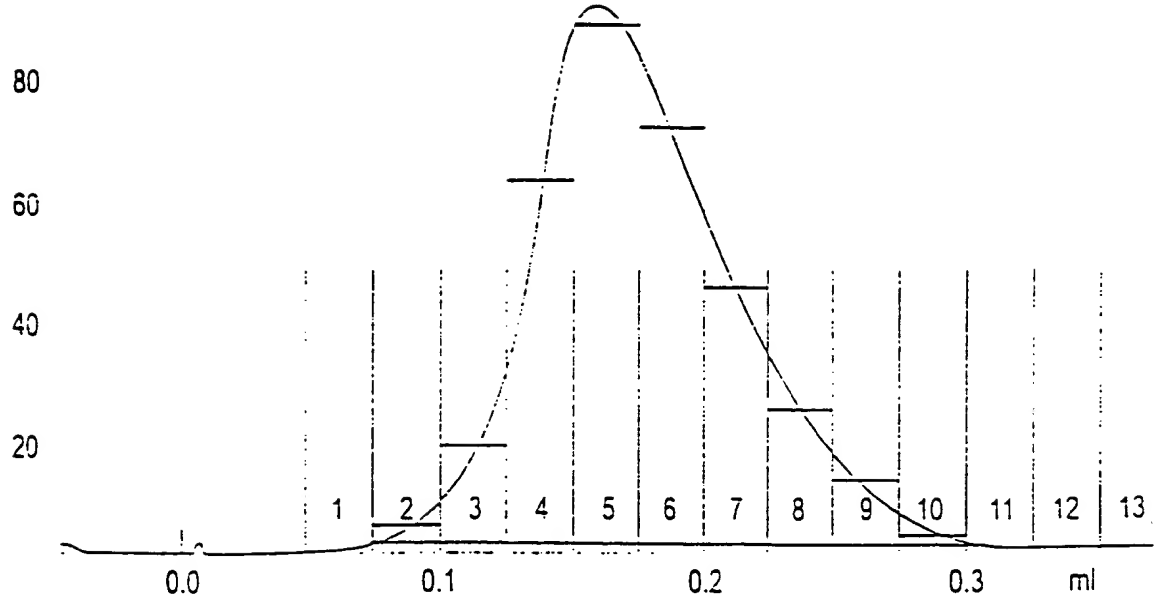
FIGURE 32

FIGURE 33:
SILVER STAIN OF PURIFIED E2



1. 30 mM IMIDAZOLE WASH Ni-IMAC
2. 0.5 ug E2

45 59 Figure 34



No.	Ret. (ml)	Peak start (ml)	Peak end (ml)	Dur (ml)	Area (ml*mAU)	Height (mAU)
1	-0.45	-0.46	-0.43	0.04	0.0976	4.579
2	1.55	0.75	3.26	2.51	796.4167	889.377
3	3.27	3.26	3.31	0.05	0.0067	0.224
4	3.33	3.32	3.33	0.02	0.0002	0.018

Total number of detected peaks = 4
Total Area above baseline = 0.796522 ml*AU
Total area in evaluated peaks = 0.796521 ml*AU
Ratio peak area / total area = 0.999999
Total peak duration = 2.613583 ml

FIGURE 35A

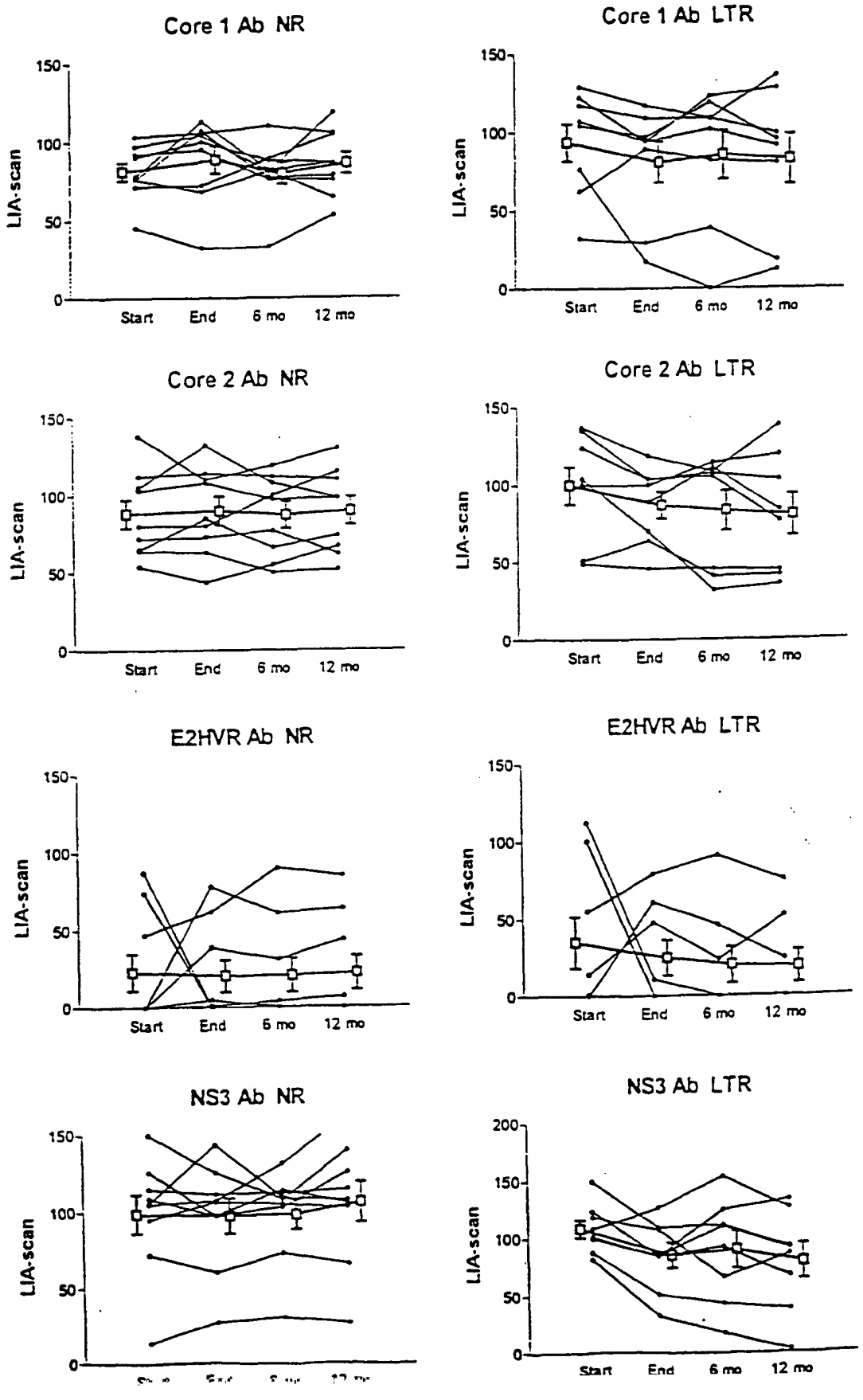

Core 1 Ab NR
Core 1 Ab LTR
Core 2 Ab NR
Core 2 Ab LTR
E2HVR Ab NR
E2HVR Ab LTR
NS3 Ab NR
NS3 Ab LTR
LIA-scan
Start
End
6 mo
12 mo

FIGURE 35B

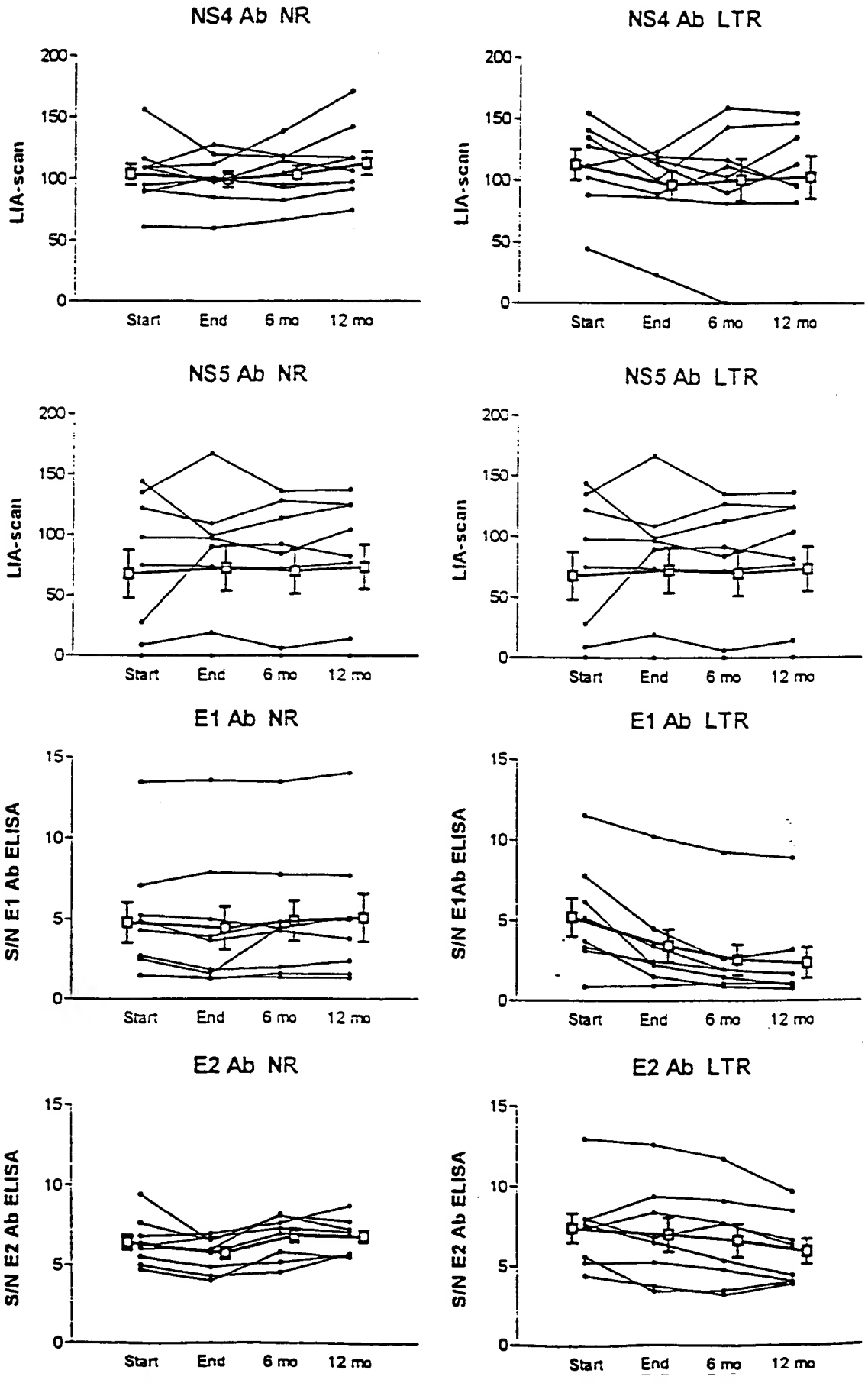
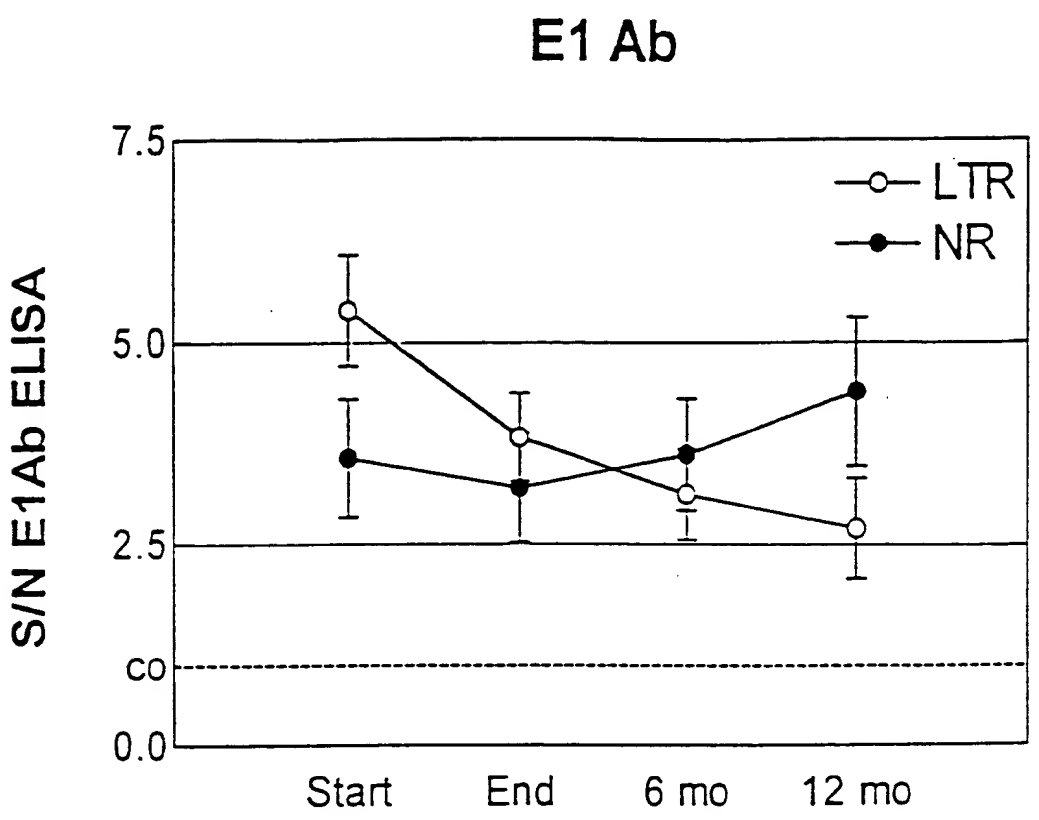

NS4 Ab NR
NS4 Ab LTR
NS5 Ab NR
NS5 Ab LTR
E1 Ab NR
E1 Ab LTR
E2 Ab NR
E2 Ab LTR
LIA-scan
S/N E1 Ab ELISA
S/N E1Ab ELISA
S/N E2 Ab ELISA
0
50
100
150
200
5
10
15
Start
End
6 mo
12 mo

Figure 36


E1 Ab
S/N E1Ab ELISA
7.5
5.0
2.5
co
0.0
LTR
NR
Start
End
6 mo
12 mo

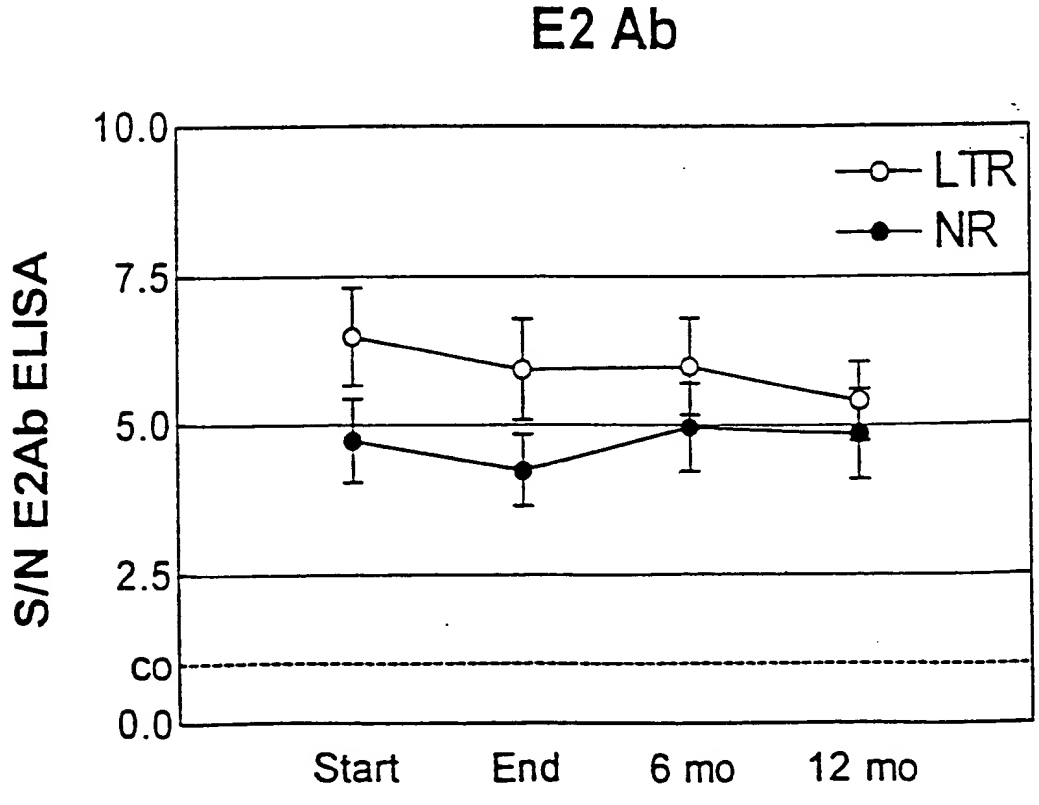

E2 Ab
S/N E2Ab ELISA
10.0
7.5
5.0
2.5
co
0.0
LTR
NR
Start
End
6 mo
12 mo

FIGURE 37

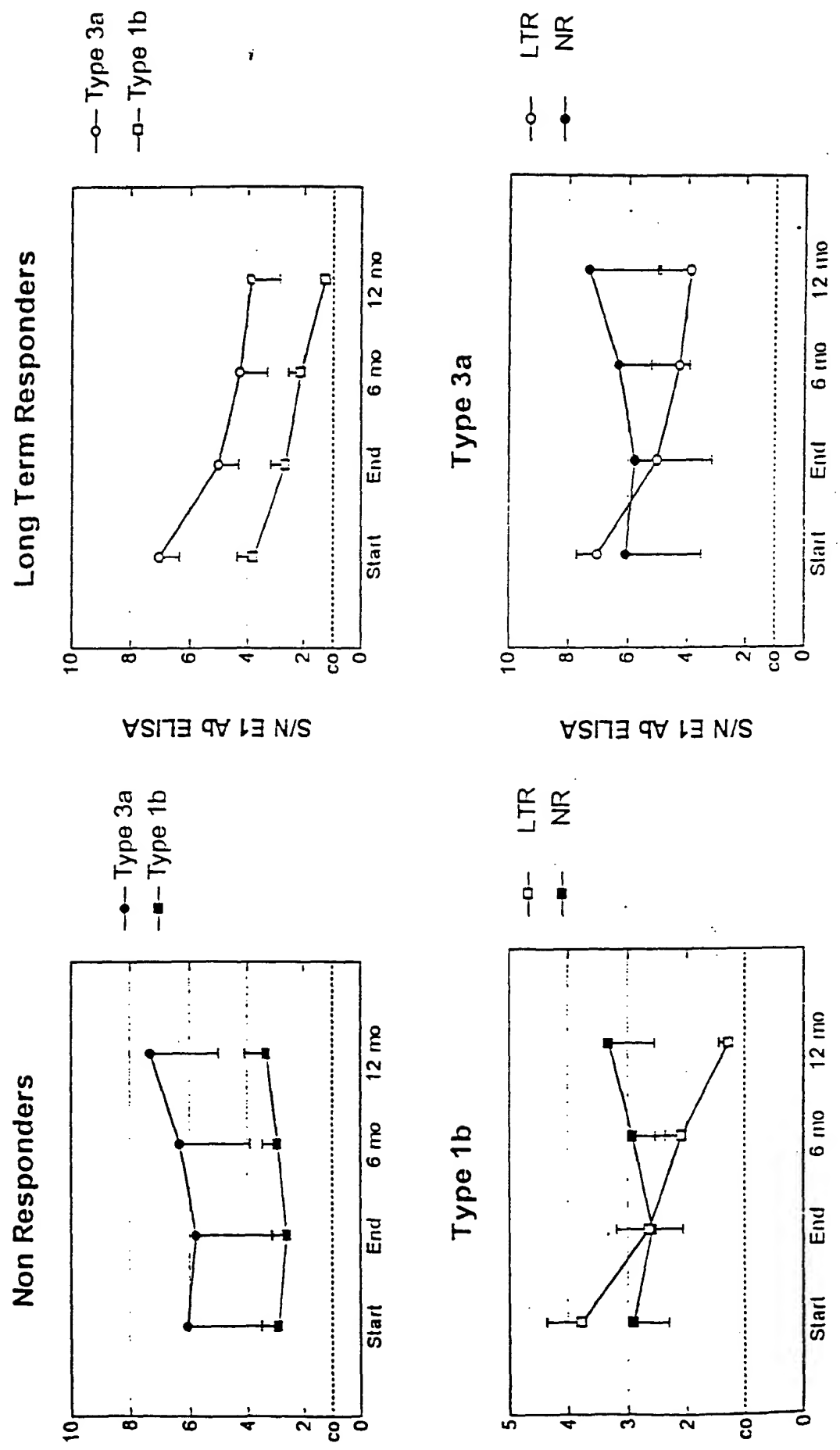
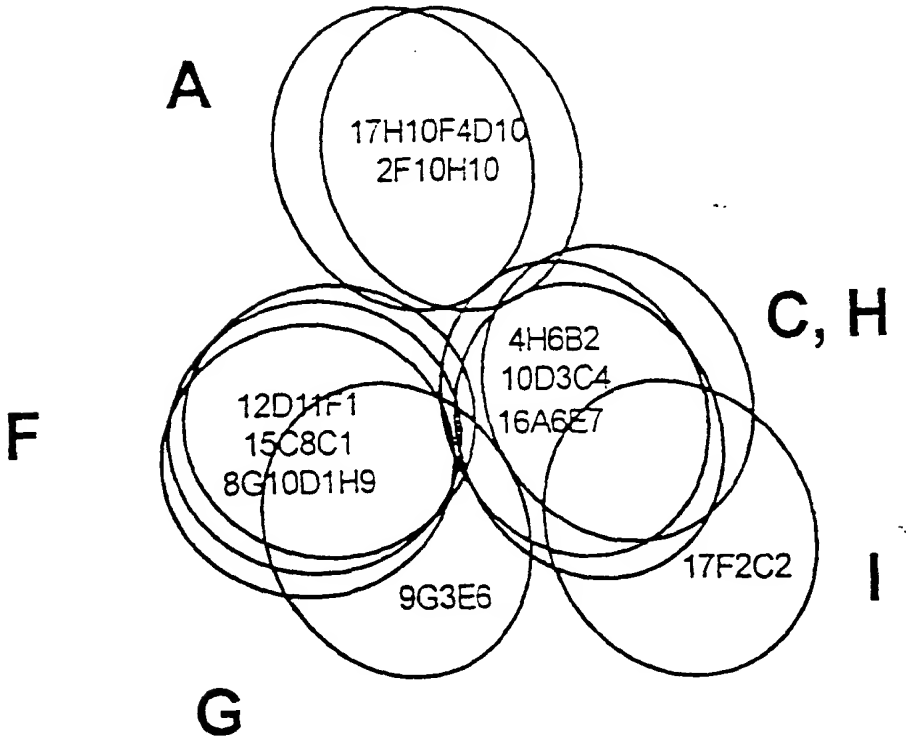

Long Term Responders
Type 3a
Type 1b
S/N E1 Ab ELISA
Start
End
6 mo
12 mo
Type 3a
LTR
NR
Non Responders
Type 1b

Figure 38

Relative Map Positions of anti-E2 monoclonal antibodies



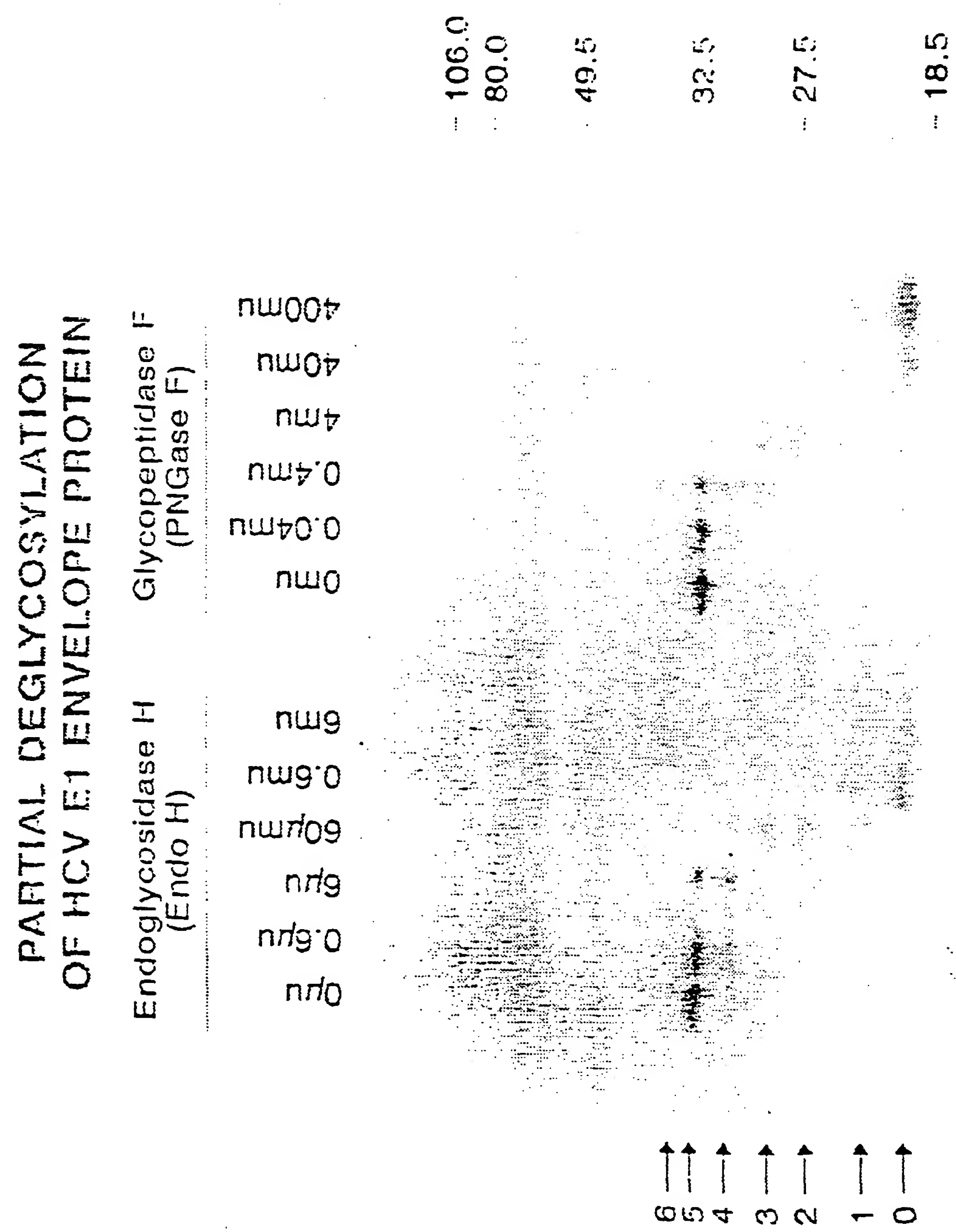

PARTIAL DEGLYCOSYLATION
OF HCV E1 ENVELOPE PROTEIN
Endoglycosidase H
(Endo H)
Glycopeptidase F
(PNGase F)
0μu
0.6μu
6μu
60μu
0.6mu
6mu
0mu
0.04mu
0.4mu
4mu
40mu
400mu
106.0
80.0
49.5
32.5
27.5
18.5
6
5
4
3
2
1
0

Figure 39

PARTIAL TREATMENT OF HCV E2\E2s ENVELOPE PROTEINS BY PNGase F

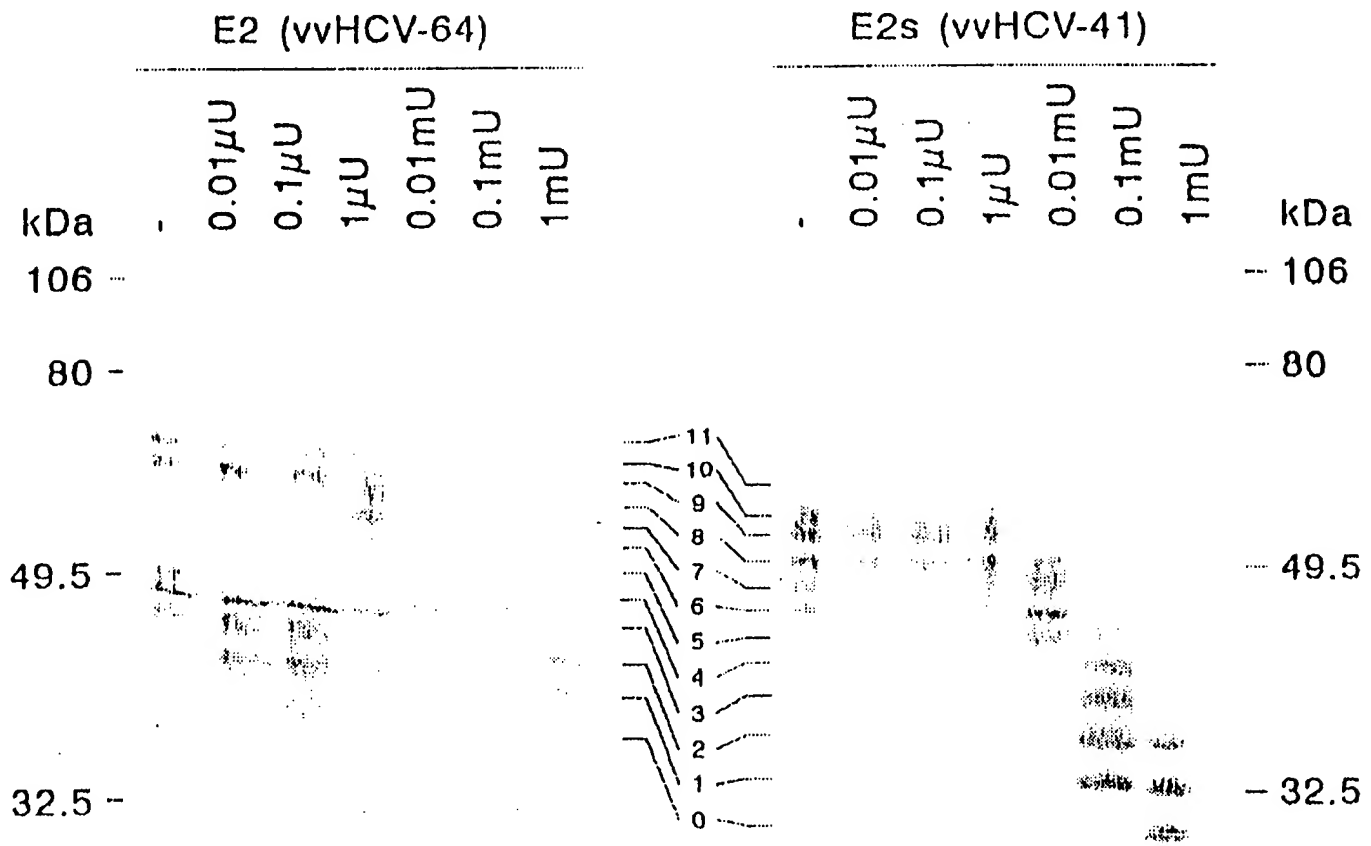


Figure 40

Fig. 41

In Vitro Mutagenesis of HCV E1 glycoprotein

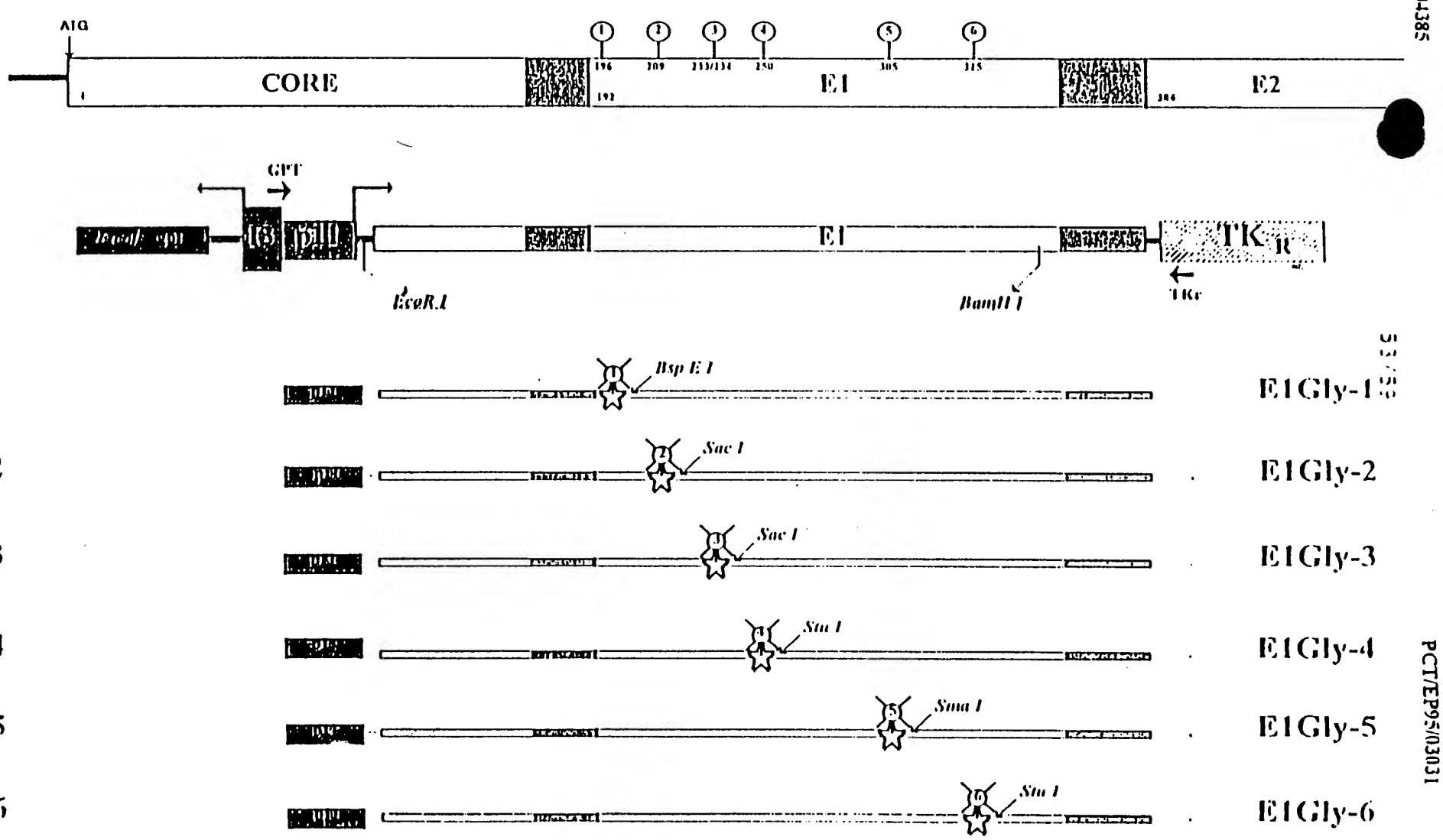
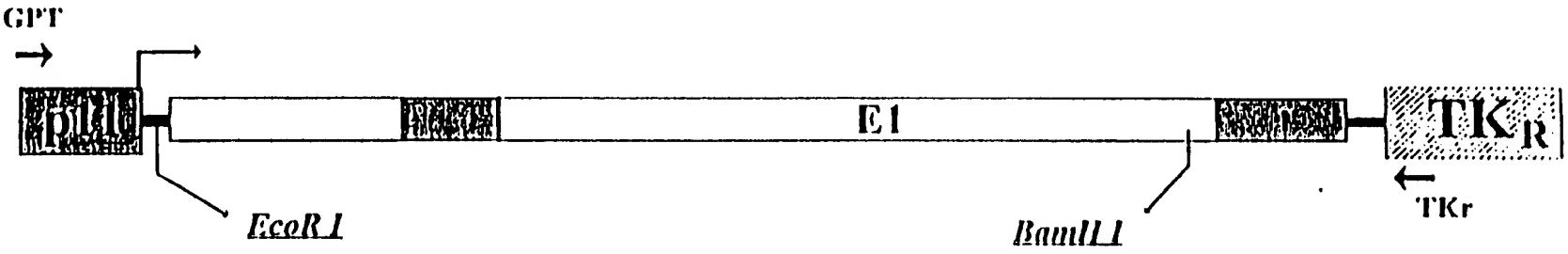


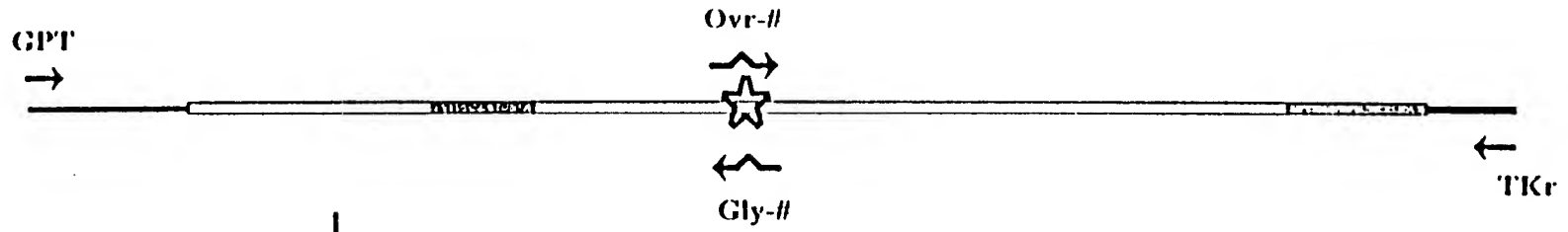
Fig. 42A

In Vitro Mutagenesis of HCV E1 glycoprotein

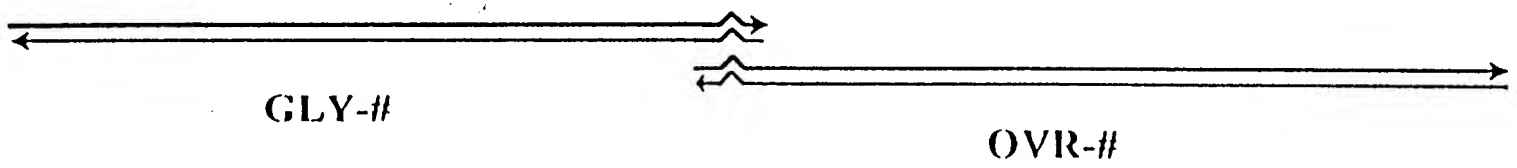
10A



1. First step of PCR amplification (Gly-# and Ovr-# primers)



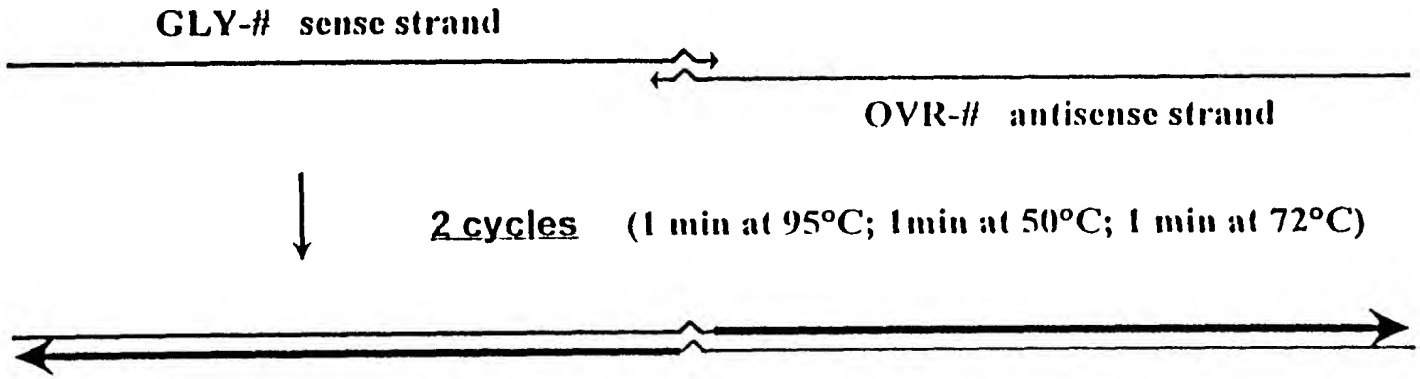
30 cycles (1 min at 95°C; 1 min at 50°C; 1 min at 72°C)



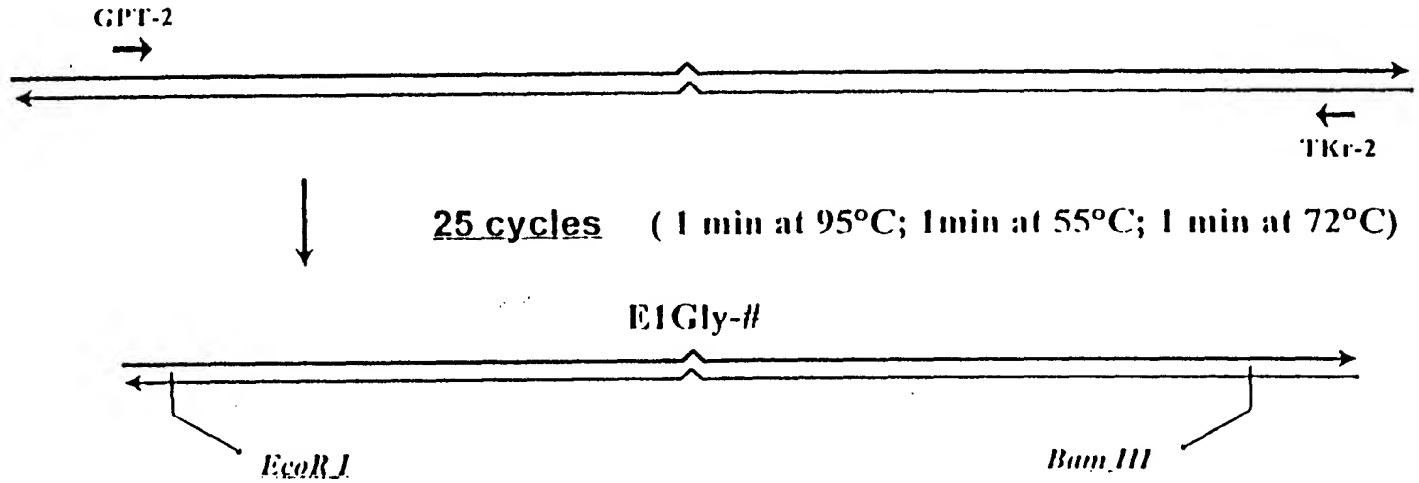
2. Overlap extension and nested PCR

Fig. 42B

a. Overlap extension



b. Nested PCR amplification (GPT-2 and TKr-2 primers)



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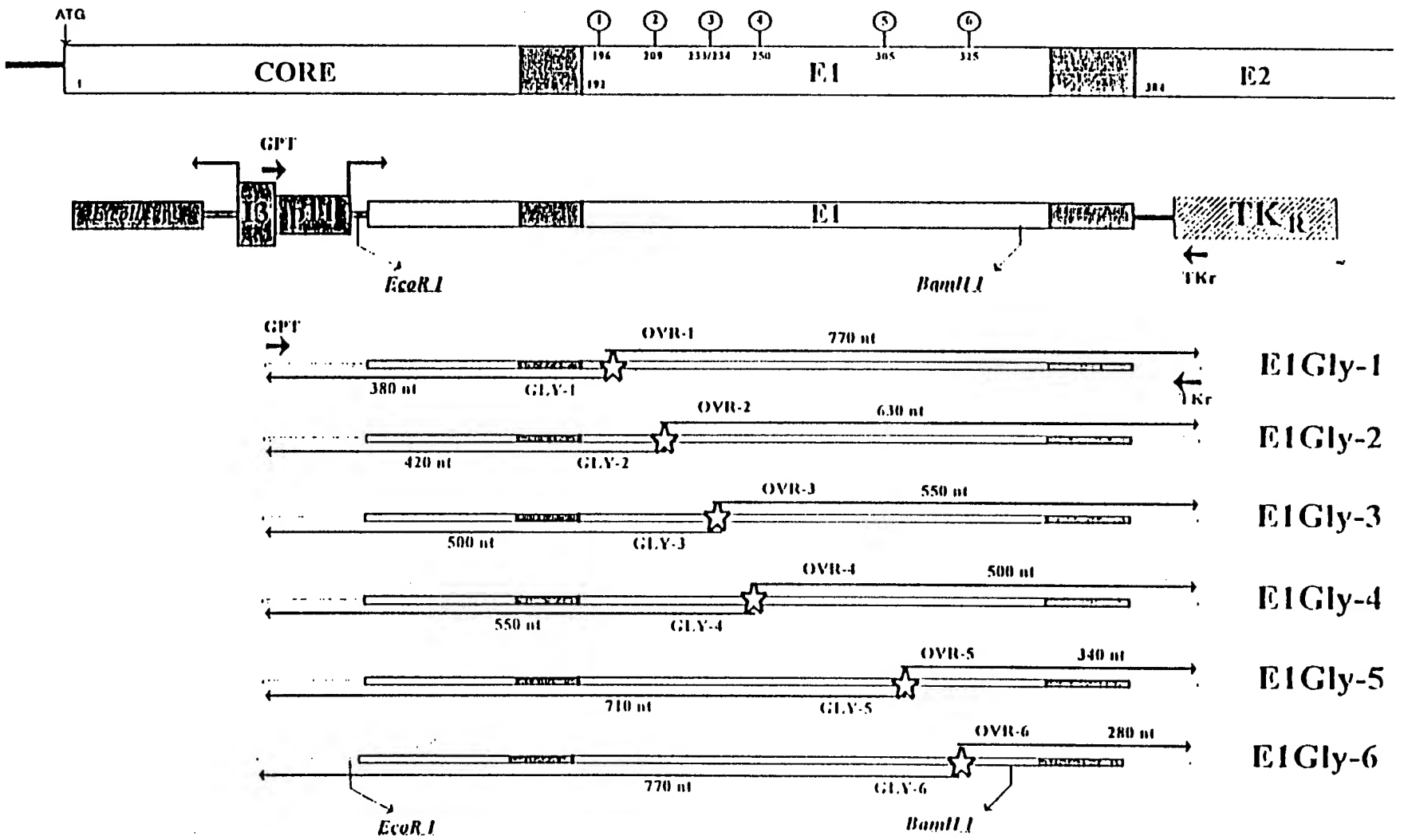
55/59
PCT/EP95/03031

Fig. 43 *In Vitro* Mutagenesis of HCV E1 glycoprotein



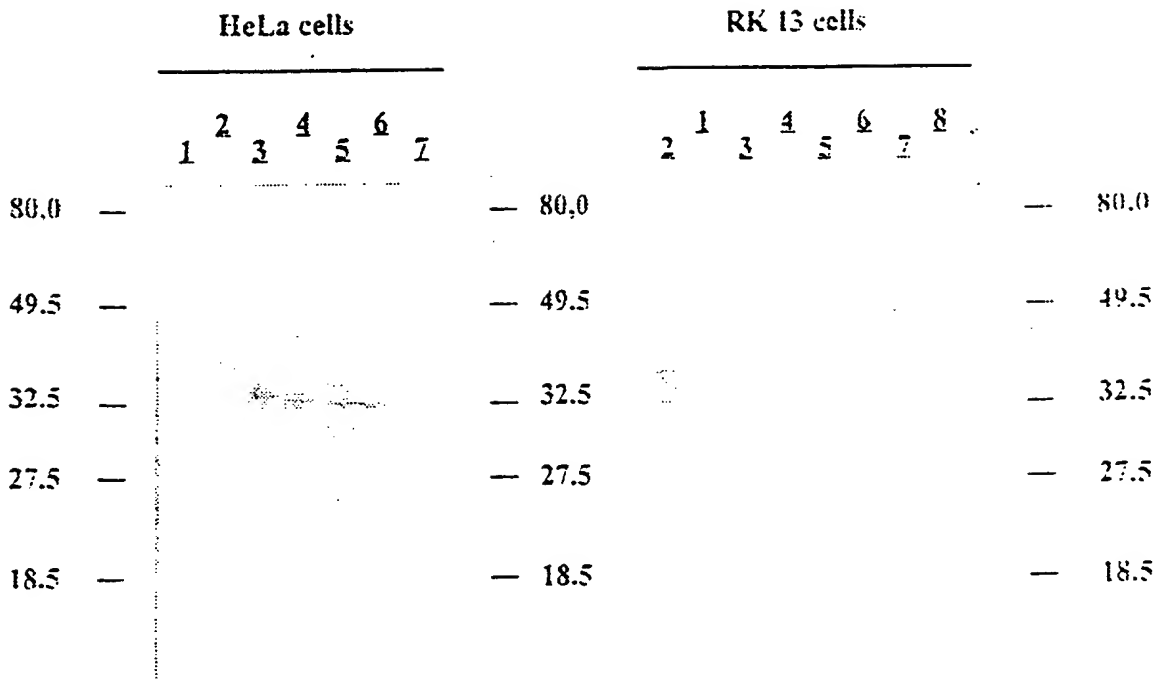


Figure 44A

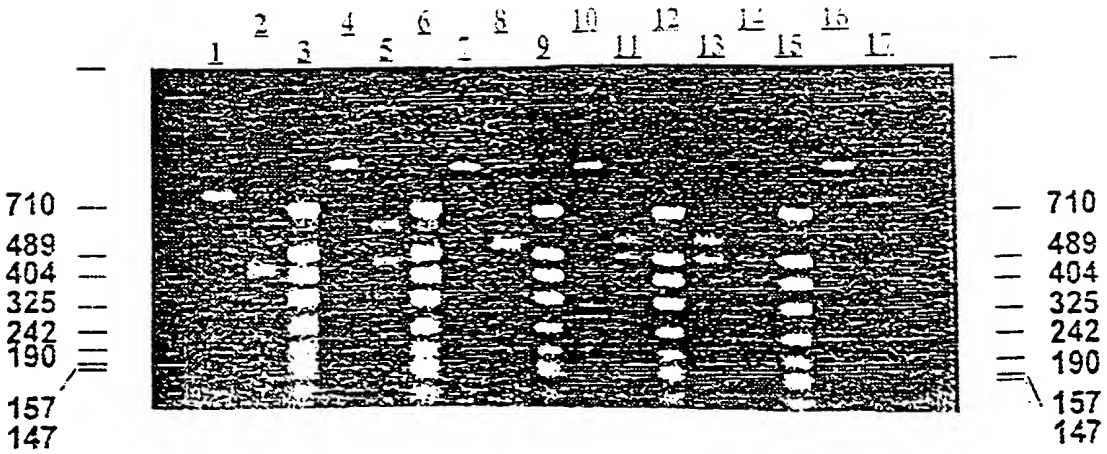


Figure 44B

Figure 45

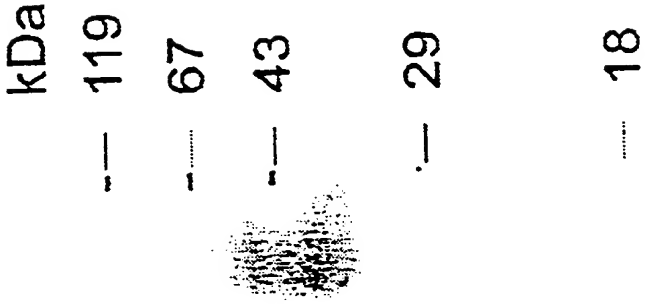


Figure 46